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ORIGINAL ARTICLES

SARCOMA OF THE STOMACH.

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The stomach is one of the most unusual sites for sarcoma. The infrequency of the lesion, and the recovery of health following an extensive resection of the stomach prompt me to place my experience with a single case on record. The first case of primary sarcoma of the stomach was recorded by Bruch, in 1847, in hsi *Diagnose der bösartigen Geschwulste;* in 1864, Virchow referred to 3 cases, while as late as 1893 Tilger was able to collect only 20 cases. From this time on additional cases have been placed on record, and recently G. Flebbe, in an exhaustive treatise on the subject, chiefly from the pathological view-point, assembled 157 cases, the larger number of which, however, were dicovered at autopsy. In the following statistics, sarcoma of the stomach appears to be a rather unusual lesion. Yates found in 800 stomach tumors only 2 per cent. were sarcoma; Drost and Wild in 423 sarcomas of various structures mention but one of the stomach. Of 840 sarcomas at the Berlin Pathological Institute there is only 1 of the stomach. Tilger mentions 4 in 3500 sarcomas. In 23 consecutive cases of primary malignant disease of the stomach, Fenwick found 2 sarcomas, Hosch 6 in 13,387 autopsies; Czerny saw 2 in 298 gastro-enterostomies, while Haberkahnt in 207 resections of the pylorus met with 3. Thus it may be said that of primary malignant disease of the stomach, sarcoma is represented in only 2 per cent., that only 0.25 per cent of all sarcomas are found in the stomach, and only 0.045 per cent. of all cases coming to autopsy.

On December 20, 1912, I saw on my service at the Episcopal Hospital, a woman (M. F., No. 4299), aged thirty-six years, whose chief complaint was vomiting and heart-burn. She had been subject to light attacks of indigestion for the past twelve years, which were promptly relieved by the remedies prescribed by her physician. The patient dates the onset of her present trouble to January, 1912, about twelve months ago, when she began to have vomiting spells accompanied with nausea or pain, coming on suddenly and without warning, usually about three hours after eating, at first two or three times a week, lately more frequently. She had never vomited any blood; had never been jaundiced, and had lost twelve pounds in twelve months. There was nothing in her family history or in her previous personal history of note save that she had had typhoid fever and smallpox. Upon examination she appeared considerably undernourished; there was a moderate pallor of the skin, but nothing unusual about the condition of the thoracic and abdominal organs other than the lesion about to be described.

Upon inspection of the abdomen, the outline of a mass about the size of a pear could be readily seen, extending across the left hypochondrium, about two inches above the umbilicus and an inch to the right of the midline. The mass rose and fell with respiration, and when grasped could be moved freely in all directions. It was firm in consistency and irregular on the surface. I was somewhat in doubt as to the source and nature of the mass. Its mobility reminded one of that of a floating kidney, although it did not appear to be in the retroperitoneal space, and its shape did not conform to that of the kidney. To determine its relation to the stomach, I percussed the abdomen before and after a draught of two tumblerfuls of water and realized at once that the tumor was in close relation with the pyloric portion of the stomach. The findings at this examination, taken with the history of vomiting, and the positive evidence of retention, determined subsequently by the raisin test, led me to make a provisional diagnosis of a scirrhous carcinoma. The history of an indigestion for over twelve years was suggestive of an ulcer period, the existence of which as a forerunner of carcinoma was not lost sight of.

The patient readily consented to an operation, which I performed December 24, 1912. Through a high right rectus incision the abdomen was opened and the tumor exposed; it involved about a third of the greater curvature, and was nearer the pylorus than the cardia. Attached to the lower margin of the growth were two loops of jejunum. The lymph nodes along the greater and lesser curvatures and about the celiac axis were considerably enlarged.

Although it seemed more than probable that the metastasis had extended beyond the first lymph-node station, and the chances of a radical cure thereby lessened, the increasing obstructive symptoms and consequent inanition justified the removal of the growth

if only for palliative purposes. I proceeded, therefore, with the operation and resected with the growth about two-fifths of the stomach. In addition a portion of the two adherent loops of the jejunum had to be excised. The operation was concluded with a posterior gastrojejunostomy and the rent in the mesocolon attached to the line of suture. The operation was bloodless, the convalescence uneventful, and the patient was discharged on the ninth day. Only recently, that is, in November, 1913, ten months after the operation, I received from the patient a letter to the effect that she was perfectly well and had regained her normal weight.

Both prior to operation and when the tumor was exposed on the operating table, I was under the impression that we were dealing with a carcinoma implanted on an ulcer base. The specimen was sent to the laboratory, and the following report revealed to my surprise that we were dealing with a lymphosarcoma:

PATHOLOGICAL REPORT.—(Dr. C. Y. White). Lymphosarcoma of the stomach; metastatic lymphosarcoma of the serous coat of the adherent loops of jejunum. The specimen, representing a considerable portion of the stomach with the tumor, is about six inches long, two inches wide, and three-quarters of an inch thick.

Mucosa: The glandular tissue of the mucosa has for the greater part been replaced by cellular infiltration. When the remaining ducts are present, they are widely separated by the infiltrating cells. Extending from the mucosa through the submucosa, the infiltrating cells form a dense layer, which is responsible to a great extent for the increased thickness of the stomach wall. In the muscular layers are to be found wide and narrow tracts of cellular infiltration. These are prominent enough to be seen plainly with the naked eye in the stained specimen.

The histology of the nodule on the serous coat of the jejunum showed a nodule of whitish color fairly firm and about the size of a walnut. Section shows the nodule to be composed of fatty tissue, fibrous tissue, and a dense cellular collection. These latter cells compose about nine-tenths of the tissue.

General consideration of the type of infiltrating cell: The cells found in the stomach wall are chiefly of the small and medium sized lymphatic type. There are, however, in the less densely packed areas, cells of larger type with a moderately large vesicular nucleus and considerable protoplasm. The majority of the cells show surrounding protoplasm. In a few areas these cells are densely packed, suggesting lymph nodes. Mitotic cells are fairly numerous throughout the section. The same type of cell is found in the nodule removed from the jejunum; here, however, they are far more numerous and very densely packed, and mitotic cells are numerous. The bloodvessels throughout the section of the stomach and the metastatic nodule are thin walled and by no means numerous. A connective-tissue frame work throughout both sections is not at all prominent and represented by thin bands.

A Series of Twenty-eight Operative Cases Arranged in Chronological Order, with Statistical Data.

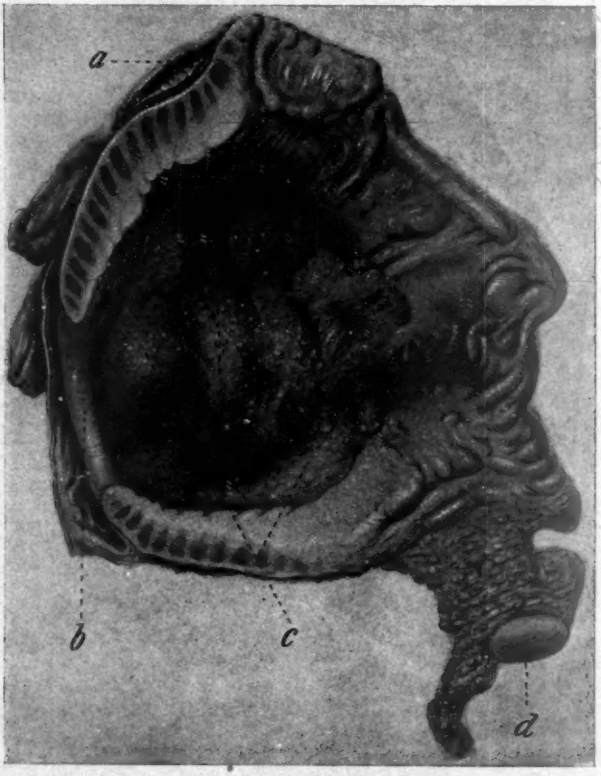
Author.	Date.	Sex.	Age.	Variety.	Site.	Metastasis.	Results.
Billroth	1888	..	..	Round-celled	Anterior wall	.....	Successfully removed.
Torök (Salaman)	1892	F.	21	Round-celled	.....	.....	Successfully removed.
Hartley	1896	F.	54	Spindle-celled	Posterior wall	.....	Successfully removed.
Morton	1899	M.	39	Round-celled	Diffuse	Duodenum	Removed. Well after two years.
Cantwell	1899	F.	52	Spindle-celled	Posterior wall	.....	Removed. Recurrence eight months later.
Finlayson	1899	M.	3½	Mixed-celled	Posterior wall	.....	Successfully removed.
Capello	1899	F.	54	Cystic	.....	.....	Well two years after.
Dock	1900	M.	55	Lymphosarcoma	.....	.....	Successfully removed.
Schoph	1899	F.	..	Lymphosarcoma	.....	.....	Well after one year.
Herman	1901	F.	60	Myxosarcoma	Greater curvature	.....	Successfully removed.
Miodowski	1903	F.	40	Large round-celled	Posterior wall	.....	Operation; death.
Bird	1903	M.	41	Mixed-celled	Pylorus	Duodenum	Recurrence three years after.
Moser	1903	F.	17	Myosarcoma	Lesser curvature	.....	Operation; death.
Moser	1903	F.	41	Myosarcoma	Posterior wall	Pancreas	Successfully removed.
Moser	1903	M.	50	Myosarcoma	Posterior wall	Adrenal	Death.
Alessandri (Salaman)	1903	F.	53	Fibromyoma	Greater curvature	.....	Successfully removed.
MacCormick-Welsh	1906	F.	53	Spindle-celled fibrosarcoma	Posterior wall	.....	Well five months later.
MacCormick-Welsh	1906	M.	62	Large spindle-celled	Posterior wall	.....	Well two months later.
Yates	1906	F.	57	Large round-celled	Posterior wall	.....	Successfully removed.
v. Eiselsberg	....	..	..	Fibrosarcoma	Fundus	.....	Successfully removed.
Yates	1906	M.	44	Spindle-celled	Posterior wall	.....	Well four and one-half months later.
Moschcowitz	1909	F.	58	Spindle-celled	Greater curvature, near cardia	.....	Death.
Maryland and Anderson	1910	F.	57	Spindle-celled	Greater curvature	.....	Recovery
Rupert	1912	F.	58	Lymphosarcoma	Diffuse	.....	Gastrectomy, 1898. Well fourteen and one-half years after.
Moschcovitz	1912	M.	50	Lymphosarcoma	Pyloris	.....	Well nine months later.
Kondring	1913	F.	35	Spindle-celled	Greater curvature	.....	Recovery.
Amelung	1913	M.	5	Myosarcoma	Pyloris	.....	Well nine months after.
Scudder	1913	M.	29	Spindle-celled	Posterior wall	None	Well eleven months after.
Frazier	1912	F.	36	Lymphosarcoma	Greater curvature	Jejunum lymph nodes	Well nine months after.

Pathologically the tumor conformed to one of the two types most commonly represented in sarcomas of the stomach. While all forms of sarcoma may be found, the small round- and spindle-celled types predominate. In an analysis of 61 cases, I found 23 spindle-celled, 16 small-round celled, 3 large round-celled, 6 lympho-sarcoma, 7 myo-sarcoma, 5 myxo-sarcoma, and 1 cystic sarcoma. In conformance, too, with the general rule, the specimen which I removed originated in the pyloric portion of the stomach, the common seat of small round-celled variety in contrast to the spindle-celled, which usually involves the fundus and chiefly the posterior wall. The spindle-celled variety is slower in growth, slower in metastasizing, more apt to be circumscribed, often becoming pedunculated, forming a round, hard; movable mass in which ulceration is rare and late. It usually springs from the submucosa and dissects its way between the mucous and muscular coats. Although more frequently found near the pylorus the round-celled does not only actually occlude its lumen, but by infiltrating the stomach wall renders it rigid and the pylorus patulous. The expulsive power of the antrum is crippled by the extensive infiltration of the muscularis, and for this reason symptoms of obstruction and retention, conspicuously represented in my own case, are often found (see illustration). The widespread and diffuse infiltration of the round-celled variety is not unlike the lesion found in lymphocythemia, and when similar lesions are found in other organs, the process in the stomach should be regarded as an expression of lymphocythemia rather than as a primary malignant growth. The round-celled type rarely gives a palpable tumor, is more rapid in its course with earlier metastasis and well-marked cachexia.

As to the most frequent sites of the tumor, some reference has already been made. Flebbe mentions 37 cases where the pylorus was reported involved, the greater curvature in 30, the posterior wall in 26, 13 on the lesser curvature, the anterior wall in 8, the cardia in 3, in 2 the pylorus and both curvatures, while in 27 cases almost the entire stomach was infiltrated.

Contrary to the belief that sarcoma is most frequently found in the young and in early adult life, an analysis of recorded cases shows that sarcoma of the stomach is more frequent in later adult life; in 35 cases collected by MacCormick and Welsh, 11 occurred between fifty and sixty years, 6 between forty and fifty, 6 between sixty and eighty, while there were but four between twenty and forty years. The youngest was three and a half years, while the oldest was eighty-five years. These results are comparable with those of Corner and Fairbanks, who found the incidence greatest between the ages of forty and fifty years. In a recent review in 17 cases by Scudder, in which the author makes the statement that gastric sarcoma is a disease of the young, 14 occurred in people over forty, while only 3 were under this age.

As with most of the unusual forms of tumors or common types of tumors in unusual sites, the true nature of the lesion is not revealed until the histological examination has been made. In the case reported, I was reasonably confident we were dealing with a carcinoma, and there was no means either of proving or disproving this preliminary diagnosis before the abdomen was opened and the



Lymphosarcoma of the stomach. The specimen represents a portion of the stomach removed for lymphosarcoma. *a*, portion of the intestine adherent to the tumor and resected; *b*, the pylorus; *c*, the seat of the tumor; *d*, lymph nodes.

specimen examined. As a matter of fact, I have been unable to find a single instance where the true nature of the lesion was known prior to operation or autopsy. The difficulties are illustrated by the case of Köndring, in a female, aged thirty-five years, who had had gastric trouble for eight months. Upon examination a fluctuating tumor was found filling the entire lower abdomen to a

hand's breadth above the umbilicus. It was thought to be a cystic ovary, but the operation revealed a primary cystic spindle-celled sarcoma springing from the posterior surface of the greater curvature near the fundus. In general terms, it may be said that given a patient presenting gastric symptoms of several months' duration, with a readily palpable, freely movable tumor of the stomach, but without the loss of weight, general debility, and cachexia common to carcinoma of the same duration, one might be justified in suspecting sarcoma.

The expectation of life varies with the duration of the lesion prior to operation and the character of the tumor. In the 28 cases tabulated in the appended table the end results are recorded in but few. The period of survival was mentioned in but 12 of these; 1 had survived fourteen years, 2 two years, 1 one year, 1 had recurrence in three years, and 8 were reported as well from two to eleven months after the operation. Naturally as elsewhere, although seemingly much later in the course of the growth, metastasis takes place. Secondary growths have attacked the mesentery, omentum, colon, small intestine, peritoneum, pancreas, abdominal wall, kidneys, pleura, lungs, ovaries, scrotum, bone, and skin. Howard found metastasis in 40 per cent. of cases, in 50 per cent. along the lymph channels, Lofaro in 50 of 123 cases, and Hosch in 39 of 85 cases. As metastasis takes place relatively late when compared with cancer, the size of the tumor and its duration should not deter the surgeon from resecting as much of the stomach as need be when this can be accomplished without undue risk.

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CRITICAL EXAMINATION OF ONE HUNDRED PAINTERS FOR EVIDENCES OF LEAD POISONING.

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At the request of Dr. Alice Hamilton, of the United States Department of Commerce and Labor, I undertook the examination of 100 able-bodied painters, based upon (1) complete family, personal, and occupational history, (2) chief symptomatic and industrial complaints, (3) physical examination, and (4) certain significant tests, with the view of establishing the prevalence of plumbism or its after-effects among them. The source of material was from a large Chicago painters' union, whose officials for some years past had been giving considerable attention to morbidity and mortality statistics among their members.

These workmen may be said to constitute the hightest type of such tradesmen to be found in Chicago as regards intelligence, industry and thrift, trade application, morality, personal hygiene, and general interest in personal and community welfare. A large percentage were of foreign extraction, rearing, and trade apprenticeship. According to the statements of these, they had used very little lead paint before coming to America, zinc being the principal foreign substitute.

The examinations were made in the six weeks' period between February 22 and April 4, 1913. By an arrangement with the men

and their officials the candidates came at stated hours to the examiner's office. Each case required about one hour's time, the examination of blood-smears and the analysis of the urine for lead being completed outside of this time. It may be stated that these examinations were made at the end of the winter's slack season, consequently all the men examined should have exhibited the minimal immediate effects of plumbism. The men were not taken from a sick list, but from those who attended the weekly meetings or were present at the business headquarters of the union.

CASE HISTORIES.

Age.

Between 20 and 25 years	7 men.
Between 26 and 30 years	14 "
Between 31 and 40 years	26 "
Between 41 and 50 years	33 "
Between 51 and 60 years	17 "
Over 60 years (62, 67, 68)	3 "
Total	100 "

Particular Trade Processes.

General painters, many doing some paperhanging	63 men.
Interior painters and decorators, some paperhanging	32 "
Exterior painters exclusively	2 "
Carriage painter exclusively	1 "
Paperhangers, doing some painting	2 "
Total	100

Nationalities.

Scandinavian born	51 men.
German born	9 "
American born	20 "
Hebrews (mostly foreign born)	9 "
Miscellaneous foreign born	11 "
Total	100 "

Time at Trade.

Two men had begun the trade at the ages of thirty and thirty-one. (With these exceptions all had begun as youths)

Less than 5 years at the trade	1 man.
Between 5 and 10 years at the trade	17 men.
Between 11 and 20 years at the trade	32 "
Between 21 and 30 years at the trade	28 "
Between 31 and 40 years at the trade	17 "
Between 41 and 50 years at the trade	4 "
For 54 years at the trade	1 man.
Total	100 men.

Began the Trade.

United States of America	48 men.
Abroad	41 "
Not ascertained	11 "
Total	100 "

Father's Occupation that of Painting in 15 cases.

Significant Family History. The age of parents, cause of death, father's occupation, number of brothers and sisters, with cause of and age at death, were inquired into in all cases. While allowing for the unreliability of laymen's statements, still the following was deduced concerning parents, brothers, and sisters;

Tuberculosis	100 inquiries,	8 positive,	4 questionable
Cancer	75 "	9 "	
Insanity and epilepsy	70 "	5 "	2 questionable

Significant Personal History.

No previous diseases (other than venereal and not including probable instances of lead poisoning)	53 cases.
Suggestive evidence of plumbism in the past based upon:	
(*a*) Physician's diagnosis	10 "
(*b*) Paralyses: both wrists	1 "
both legs	1 "
(*c*) Appendicitis (1 questionable)	2 "
(*d*) Encephalopathy (epileptiform seizures, delirium or unconsciousness without fever or other diseases than probable plumbism) (2 others questionable and 1 further, which was undoubtedly due to methyl alcohol.)	3 "
(*e*) The "lead triad" (abdominal colic, obstinate constipation, severe headache without fever, with or without vomiting, all of these coming in "spells" or attacks lasting a couple of days or more and without other assignable cause) (2 others questionable.)	32 "
(*f*) "Rheumatism" (as lumbago, sciatica, pleurodynia, brachialgia, etc.), excluding cases of rheumatic fever, nerve traumatism, etc.	51 "
(*g*) Statements as to previous existence of lead-line in gums were discarded as unreliable.	
(*h*) Negative evidence of any of the above conditions	27 "
(*i*) Positive evidence of one or more of the above conditions	73 "
Serious accidents	24 "
Serious operations (2 appendicitis, 4 hernia)	6 "
Serious diseases:	
Typhoid	18 "
Pneumonia	11 "
Malaria	11 "
Pleurisy	8 "
Infections (2 smallpox)	3 "
Inflammatory rheumatism	4 "
Tuberculosis (1 questionable)	3 "
Bronchitis	2 "
Nephritis	1 "
Multiple lipomata	1 "
Wood-alcohol blindness (partial in 2 cases, recovery complete in 1 case)	3 "
Jaundice	1 "
Venereal diseases:	
Not ascertained	10 "
Denied	49 "
Gonorrhea	32 "
Chancroids	9 "
Syphilis (3 others questionable)	4 "

Habits. The approximate extent of the consumption of beverages, etc., was inquired into by ascertaining the number of cups or "drinks" per day. None admitted the use of habit-producing drugs, and there was no evidence of same. In the following table

the term "moderate" has the following applications: in the case of tea or coffee, the use of not over four cups per day; in the case of beer, not over three glasses per day; in the case of whisky, not over two "drinks" per day.

Beverage.	None.	Occasional.	Moderate.	Excessive.
Tea	41	27	32	0
Coffee	7	7	73	13
Beer	10	34	42	14
Whiskey	22	52	20	6

I believe that these figures are fairly accurate, also that the tendency to moderation among the 100 men examined is rather better than for the average tradesmen.

Marital History.

Single (always)	24 men.
Married or widowers	76 "
Married one year or more	74 "
Wives never pregnant	11 "
Pregnancies but no living progeny	10 "
With living progeny	53 "
Statistics on miscarriages, no certain information.	
Association between wives washing leaded garments and miscarriages, no certain information.	

Progeny.

1 child living	14 men.
2 children living	18 "
3 " "	12 "
4 " "	5 "
5 " "	2 "
6 " "	2 "
8 " "	2 "
Total living children of 74 men, married at least 1 year	144
Average " " 74 " " 1 "	1.95

Progeny and Age of Married Men. There were 49 married men of forty years of age or over, of whom 37 had living progeny.

There were 35 married men of forty-five years of age or over, of whom 26 had living progeny, whereas 7 had had none at all. In this group 2 had a total of 28 children with 16 living. The total progeny of the group was 116 children, or an average of 3.31 each; total living progeny was 75 children, or an average of 2.14 each; this includes the two large families, without whose statistics the respective averages would be 2.67 and 1.79 each. This is certainly very low for married men of at least forty-five years of age. Analysis showed that these same 35 men with their total of 116 living and dead progeny came from families having a total of 235 offsprings. While this group of forty-five-year-old painters may have more progeny, it is not likely they will double the same, as would be necessary to equal their own ancestral average.

Just what part lead poisoning and what part various social conditions may have had to do with this decreased progeny is impossible of ascertainment.

COMPLAINTS.

(*a*) *Hygienic Complaints and Comments.*

Breathing lead paint dust from sandpapering	99 cases.
(Inquiry showed the men would have no objection to substituting zinc for lead)	
Sickened by turpentine in close quarters	64 "
Sickened by benzine in close quarters	70 "
Sickened by "hard-oiling," practically all cases.	

The men complain most bitterly of the effects of "hard-oiling" upon sensorium, skin, and digestive tract; less so of turpentine upon the digestive tract, sensorium, and bladder; and least of benzine upon sensorium, occasionally upon the digestive tract.

Wood alcohol has been largely displaced by denatured alcohol, according to their statements. Few men claim that they use either to any particular extent. Those who had been blinded had been performing special work, as in brewery vats, etc.

Other frequent complaints, particularly of respiratory, skin, and stomach disturbances, were: varnish removers, ammonia and lyes, fusel oil, oxalic acid, muriatic acid, acetone, amyl-acetate, creosote, naphtha, and various patented "dope" varnish-and-paint removers.

Time at noon hour: This was invariably one-half hour, although many stated that by special arrangements with their employer one hour might be had, providing an extra half-hour were added at the end of the day. Many said they would prefer this, as the half-hour noon-time was insufficient for properly washing up, eating, etc. *Working day* was eight hours (8 A.M., to 12 noon; 12.30 to 4.30 P.M.).

Washing of hands before eating: All the men questioned claimed a knowledge of the danger of lead poisoning from paint on hands. All stated they endeavored to wash hands with soap and water where possible; occasionally one carried his own soap and towels; most resorted to benzine to remove the paint, while a number claimed that they always ate their sandwiches, pie, etc., held in pieces of paper. Few gave much attention to the lips.

Mustaches: Fifty inquiries showed that these were worn constantly in 18 cases, occasionally in 7 cases, and not at all in 25 cases. Beards were not encountered. Only a few men had considered deposition of paint and dust in mustaches and the possibility of straining drinks through same as dangerous. Some considered that they protected nasal breathing; this is certainly a wrong impression.

(*b*) *Present Health Complaints.* The following list of symptoms, embracing those most commonly occurring in acute or chronic plumbism, was inquired into in the case of each of the 100 men. They may be considered as the complaints of the past few weeks or months:

Symptoms.	Severe.	Moderate.	Slight or occasional.	Total.
Loss of strength	..	12	4	16
Loss of weight	..	9	3	12
"Nervousness"	5	19	9	33
Digestive:				
Nausea	1	14	1	16
Anorexia (morning)	3	13	8	24
Foul taste	4	17	12	33
Foul breath	2	7 (?)	?	9 s.c.
Salivary disturbances	2	16	?	18 s.c.
Emesis	..	6	4	10
Constipation	15	19	16	50
Diarrhea	2	8	9	19
Melena	..	2	3	5
Hemorrhoids	5	13	10	28
Visceralgia	9	18	16	43
Colic	..	4	3	7
Distention	8	18	9	35
Sensorial:				
Headache	17	14	19	50
Vertigo	4	19	13	36
Syncope	..	2	4	6
Insomnia	4	6	12	22
Nightmare	1	5	5	11
Depression	1	3	4	8
Confusion	..	6	2	8
Memory failing	s.c.	14	7	22
Neuromuscular:				
Neuralgia	1	3	2	6
Arthritic pains	3	10	11	24
Anesthesia and paresthesia, especially of arms	2	18	6	26
"Rheumatism"	1	18	16	35
Muscular cramps	1	12	11	24
Trembling	2	7	8	17
Ocular (especially "spots" and diplopia)	6	17	7	30
Itching eyelids	1	8	5	14
Aural (tinnitis, deafness)	4	23	13	40
Urinary (incontinence, nocturnal frequency)	7	27	4	38
Genital (impotence)	1	3	3	7
Circulatory (palpitation, epistaxis)	..	12	15	27
Festering cuts	..	1	1	2
Neurasthenic	1	5	9	15

Special symptoms associated with severe or acute plumbism, such as psychoses, paralyses, paroxysms, aphonia, etc., were not encountered.

Comments on the Above Table. So far as possible, specific causes of any of the above symptoms, other than lead poisoning, have led to the exclusion of such symptoms in the above table, that is, (1) in cases of rupture, visceralgia, constipation, and distention were omitted; (2) neuralgias due probably to teeth were omitted; (3) joint pains and "rheumatism," due to acute inflammatory rheumatism, past or present, were omitted; (4) defective vision, due to refractive errors, omitted as far as possible; (5) aural disturbances, due to otitis media, omitted so far as possible; (6) urinary disturbances were in nearly all cases due to nocturnal frequency, not to venereal diseases, and rarely to incontinence; most cases occurred in those of advancing years; only one due to diabetes.

PHYSICAL FINDINGS.

The following scheme was carried out in each of 100 cases, with abnormal findings as listed:

	Cases.	Remarks.
General:		
Appearances unhealthy	10	
Pallor	7	Not marked in any.
Emaciation, general	4	Not marked in any.
Emaciation, local (arms)	5	Not sought for in but 25 instances.
Prematurely aged	8	
Loss of expression	1	
Loose teeth	18	
Lead line	19	10 not pronounced.
Pyorrhea	51	Pronounced in 17.
Tremor, lips or tongue	27	
Tremor of hands	19	
Deafness	4	All rather pronounced.
Nystagmus	4	
Mydriasis	12	
Myosis	2	
Unequal pupils	4	
Argyl-Robertson pupil	2	Neither with absent knee-jerks.
Ptosis	1	
Strabismus	4	All since early childhood.
Conjunctivitis	4	Rather marked in one.
Atrophic nails	1	
Wrist tumor (no injuries)	2	1 ganglion, 1 small bone; no typical Gubler tumor.
Pulse-rate	5	All arrhythmias.
Pulse-tension	..	See blood-pressure below.
Arteriosclerosis (radial)	11	
Incoördination (arms)	17	1 well marked, 6 moderate, 10 slight.
Wrist reflexes	4	2 absent, 2 markedly increased.
Wrist paralyses	0	
Chest:		
Heart abnormal	23	Including 2 questionables.
Lungs abnormal	20	7 emphysema, 1 acute bronchitis, no pronounced tubercular lesions, although 14 were suspicious.
Mediastinum	1	Dulness with tenderness.
Abdomen:		
Enlarged liver	6	
Hernia	6	
Distention (gaseous)	7	Including 1 hernia, 1 ascites.
Superficial tenderness	0	
Deep tenderness	2	1 gall-bladder?
Operation scars	8	4 hernia, 2 appendix, 2 genital.
Abdominal reflex absent	12	
Genitalia:		
Hydrocele	2	
Undescended testicle	1	
Cremasteric reflex absent	26	
Retraction of testes	7	
Skin:		
Dryness	2	1 ichthyosis.
Dermatitis	6	Mostly wrists.
Acne	6	
Dermographia	1	Very marked.
Extremities:		
Gouty toe-joint	8	
Edema of ankles	7	6 with varicose veins.
Epitrochlear glands	2	Out of 50 examinations.
Knee-jerks abnormal	16	3 absent, 13 exaggerated.

SPECIAL TESTS.

1. *Sodium Sulphide Skin Application.* This was made in 90 cases, using a 5 per cent. solution by means of an applicator. The test usually shows positive on the hands, wrists and forearms of any who have worked in lead, particularly painters, within a week or ten days, that is, a brown or black streak resulting immediately after the application. In all of my cases the hands and arms had been washed with soap and water, in many cases for a period of over several days, since the workman's last exposure to lead paint or dust. It appears that the oil and turpentine in the paint, as well as benzine used by the men to cleanse the skin, cause the paint to infiltrate the deeper layers of the epidermis and probably the follicles and skin glands to such an extent that the normal slow exfoliation is necessary to remove it. DuMoulin's test,[1] although based upon an incorrect assumption as to its value, is an amplification of this means of proving the presence of lead. Of course, other black sulphides, as copper, mercury, bismuth, nickel, and cobalt, had to be ruled out, but usually none of these concern painters. The test demonstrates to the painter himself in a very striking manner the extent to which he is actually encased in a sheet of lead, despite his soap-and-water ablutions. Out of 62 men who reported they had worked at least an hour or more with lead paint or its dust within the previous two weeks, this test was positive on hands, wrists, and forearms in 42 instances. Continuing the applicator up the arm and down the chest to the umbilicus, 6 were positive all the way; in other words, such men were practically entirely encased in a sheet of lead buried deep in the skin. I will not attempt to enter into the discussion as to the probability of absorption from this source.

2. *Urinary Analysis.* The cursory analysis was made from a fresh specimen in each case. In addition, most of the men, in response to a special request, brought a pint bottle of urine, which, being added to that part of the fresh specimen not required for immediate tests, gave several hundred cubic centimeters for the determination of the presence of lead. Of course, twenty-four-hour specimens would have been more satisfactory, and on this account the urinary features of contracted kidneys had to be omitted. Specific gravity, color, turbidity, and reaction were first determined in each sample. Albumin was sought for by the heat and acetic acid tests and by Heller's test. Reducing bodies, by Haines' reagent, supplemented by Nylander's test when indicated. Indican by Obermayer's and Lavelle's methods preceded by the lead subacetate preparation. In the remaining urine, lead

[1] Bull. de l'académie royale de Médecine de Belgique, 1884, p. 1093.

was sought for in 39 cases, selected as being the most promising although in all of these more urine should have been taken.

I am indebted to Dr. F. M. Meixner for the lead analyses, which were made with special equipment in the laboratory of the Cook County Hospital. Briefly stated, possible lead combinations in the urine were decomposed by adding to the specimen about one-tenth its bulk of pure nitric acid, boiling down to 60 c.c., filtering, washing residue, and the total filtrate of about 90 c.c. subjected to electrolysis in a properly covered lead-free beaker. By means of three dry cells arranged in series, connected up with a miniature rheostat, and a double-pole switch, a current of two volts at a milliampèrage of about 4 was maintained for a period of 8 hours in the solution, using platinum electrodes coiled in spiral form. The beaker was kept at 37° to 40° C. by an electric bulb. A browning or blackening of the electrode attached to the carbon pole gave presumptive evidence of lead, deposited as the peroxide, which was determined quantitatively by comparing the weight of the dried electrode before and after the electrolysis, also by colorimetry, and qualitatively by the usual methods. Three control experiments to determine delicacy of the method showed:

Dilution.	Percentage recoverable		
	Experiment 1.	Experiment 2.	Experiment 3.
1 to 100	99.8	99.7	96.0
1 to 500	99.4	99.7	96.8
1 to 1,000	99.7	99.4	97.3
1 to 5 000	95.2	92.0	90.0
1 to 10,000	(blackening of electrode but weights and therefore percentages not determined).		

The above results were obtained by using the required amount of lead salt to make the dilution in 500 c.c. water.

The more significant results of the urinary analysis in brief were as follows:

Acid reaction (usually sharp)	95 cases.
Albumin plus casts	7 "
Dextrose	1 "
Indican found to be increased	19 "
" " excessive	8 "
Lead present (0.16 and 0.11 mg.) traces (?) in some others	2 "

3. *Blood Examination.* (*a*) A blood-smear was made in each case and afterward stained by Harlow's solution.[2] These were examined for evidence of blood dyscrasias, basophilic erythrocytic degenerations, differential counts, etc. Briefly stated, no blood diseases were found and no evidence of severe anemias. There was an apparent slight leukocytosis present in 5 cases, many showed a tendency to mononucleosis, while Grawitz's

[2] Emery R. Hayhurst, Blood-smears, their Preparation and Staining, Jour. Amer. Med. Assoc., December 4, 1909, liii, 1909 to 1911.

granulations or stippling of the red cells was not encountered in sufficient amount to be of significance. The absence of the latter was not surprising, inasmuch as no acute cases of plumbism were encountered.

(*b*) No cases of marked pallor being encountered, the hemoglobin was estimated in each case by using simply a Tallqvist scale, the results showing:

105 per cent.	4 cases.
100 "	51 "
95 "	42 "
90 "	3 "

(*c*) Liebermann's erythrocytic resistance test,[3] which, according to Orban,[4] is markedly raised in cases of plumbism (that is, during the phase of actual intoxication the red cells become resistant to hemolysis in hypotonic salt solutions), was made in 21 selected cases, 2 of which were positive (failed to show appreciable hemolysis in 0.45 per cent. NaCl solution).

4. *Strength of Hand Grip.* This was determined by a hand dynamometer of the Collin type having a graduated reading from 0 to 200 upon the "eschelle de traction." The instrument was standardized by obtaining the records of 55 men pursuing all manners of trades and avocations except those of lead exposure; the low reading was invariably over 150 in the weaker hand, the majority of normal men showing a strength of 160 to 230. To get uniformity of conditions, each person was required to stand erect with both arms horizontally outstretched while the hand holding the dynamometer was rather slowly contracted to maximal power, then released. Enough tests were made in each case to be certain maximal power was attained, then the highest reading accepted, gripping alternately with each hand.

The results in painters showed weakness in grips of both hands in 41 of 95 cases. The strength of those ranged from 78 to 150; five other cases were discarded because of previous injury to the hands or arms.

These cases with weak grips showed significant associated conditions and findings as follows:

1. Age: 16 of 20 cases over fifty years of age.
2. Time at trade: 16 of 21 cases over thirty years at trade.
3. History of paralysis: 2 of 2 cases.
4. History of plumbism: 10 of 10 cases.

[3] L. v. Liebermann and F. v. Fillinger, Ueber Resistens der Erythrocyten bei gesunden und kranken Menschen, nebst einer einfachen Methode zu ihrer Bestimmung, Deutsch. med. Woch., 1912, xxxviii, No. 10, s. 5.

[4] Ueber gewerbliche Vergiftungen mit Bezug auf die Liebermannsche Blutprobe, Deut. med. Woch., October 31, 1912, xxxviii, No. 44, s. 3. Note also E. Schaeffer, Fehlerquellen bei Bestimmung der Resistens der Erythrozyten nach v. Liebermann und v. Fillinger, Deutsch. med. Woch., October 3, 1912, xxxviii, No. 40, s. 2.

5. History of appendicitis: 2 of 2 cases.
6. Unhealthy appearance: 8 of 10 cases.
7. Emaciation of arms: 5 of 5 cases.
8. Inguinal hernia (past or present): 7 of 9 cases.
9. Absent abdominal reflex: 11 of 12 cases.
10. Absent knee-jerks: 3 of 3 cases.
11. Low systolic pressure: 3 of 3 cases.
12. Drop in systolic pressure after exercise: 4 of 4 cases.
13. Too great a relative proportion of the following cases was also associated with weak grips: Interior painters, Germans, Hebrews, history of encephalopathy, father a painter, alcoholics, loss of strength, loss of weight, anorexia, bad taste, salivary disturbance, distension of abdomen, headaches, vertigo, syncope, insomnia, confusion, poor memory, muscular cramps, trembling, incontinence of urine, nocturnal frequency of urination, premature age, lead deposit in gums, arteriosclerosis, incoördination, absent wrist reflexes, dermographia, lead in urine, atypical blood-smear pictures, decreased percentage of hemoglobin, increased red-blood cells, resistance to hypotonic salt solutions, weakness in wrist extention, and high pulse pressure.

5. *Strength of Wrist Extension.* This was determined also by the dynamometer. The subject was requested to sit in an arm-chair, first with hand passively flexed over forward end of the arm of the chair, when, with a wet towel folded up and placed on the dorsum of the hand to keep instrument from causing pressure pain to the hand, and also to prevent its slipping, the subject was asked to raise his hand up against the examiner's resistance on the dynamometer (active resistance). This gave one reading, the minimal for which was ascertained as not less than 30 with normal men. Secondly, the subject was requested to support his forearm on the arm of the chair, with hand extended free in the air, the wet towel applied as before, after which the examiner, with instrument in hand, forced the subject's hand to flex downward against his passive resistance. This gave a second reading, the minimal for which was ascertained as not less than 35 with normal men.

The results with painters showed:

Active resistance below normal in	16 of 96	cases	in	both wrists
" " "	20 of 96	"	right	"
" " "	22 of 95	"	left	"
Passive " "	7 of 81	"	both	"
" " "	13 of 81	"	right	"
" " "	20 of 81	"	left	"

It is worthy of note that these painters were relatively stronger in the left hand and forearm, the one least used, than in the right; also that weakness in grip (prehension) was much more frequent and pronounced than weakness in wrist extension. These facts

tend to support Edinger's exhaustion theory that fatigue determines the localization of the effects of plumbism: the painter has a constant, firm grip upon his brush, while wrist movements are second, upper arm movements third, and elbow movements fourth in order of use. In acute lead paralysis it appears that the wrists are affected most and the upper arms second, therefore corresponding to range of movement in neuromuscular effort; but it appears from these tests that weakened prehension, not necessarily paralysis, is always an associated and probably the earliest condition.

6. *Blood-pressure.* This was determined with a mercury manometer (Mercer type) applied to the right arm, with the subject in a sitting posture, using the stethoscope applied to the cubital fossa to interpret the results. By this means the systolic pressure was first taken, then the diastolic, after which the patient was requested to perform a uniform exercise; namely, that of bending forward, if possible to touch the toes, and rising erect ten times. Thereafter he seated himself at once in the chair at the instrument and pressures were again determined.

Results. *Systolic Pressure:* Before exercising, and taken toward the end of the examination in each case so as to eliminate the psychical factor as much as possible; also after the patient had seen the preceding case so examined when possible. The cases ranged between 98 and 204 mm. Hg. as follows:

Not over	100 mm. Hg. in	3 cases.
Between 101 and 120	"	39 "
Between 121 and 130	"	17 "
Between 131 and 140	"	17 "
Between 141 and 150	"	12 "
Between 151 and 160	"	6 "
Over 160	"	6 "
Total		100 "

From the above it will be seen there were 41 cases in which the systolic pressure was 130 or above (meaning an unfavorable prognosis, according to Blum[5], if continuously so, and implying contracted kidneys). However, if we take Johnston-Lavis'[6] observation that the systolic pressure should not be over the number of years of age plus 100 for adults—there were 19 cases abnormal. Of these 19 cases, 16 had a significant disqualifying history: syphilis (2), excessive coffee drinking (4), excessive alcoholic consumption (8), valvular heart disease associated with inflammatory rheumatism (2).

[5] Medinische über die Bleivergiftung. Deutsch. med. Woch., April 4, 1912, xlviii, No. 14. Blum also advises absolute prohibition from the trade if blood-pressure is continuously above normal.

[6] Sphygmomanometry and Pachon's Oscillometer, British Med. Jour., January 13, 1912, No. 2663, p. 72.

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Thirty-five cases in which systolic blood-pressure was 132 mm. or over showed significant association as follows:

1. Age, 10 of 20 cases over fifty years old.
2. Time at trade, 12 of 22 cases over thirty years at trade.
3. History of encephalopathy, 4 of 5 probable cases.
4. Alcoholics to excess, 21 of 27 cases.
5. Arteriosclerosis (radial), 8 of 11 cases.
6. Wrist reflex absent, 2 of 2 cases.
7. Abdominal reflex absent, 10 of 12 cases.
8. Knee-jerks absent, 3 of 3 cases.
9. "Gouty" great toe-joint, 6 of 8 cases.
10. Albumin and casts, 5 of 7 cases.
11. There was also associated too great a relative proportion of the following complaints and afflictions: History of plumbism, history of "triad," history of rheumatism, history of coffee excess, loss of weight, vomiting, constipation, diarrhea, visceralgia, distention of abdomen, headaches, depression, poor memory, joint pains, muscular cramps, "rheumatism," tinnitus aurium, urinary and circulatory disturbances, premature old age, pyorrhea, tremor, incoördinations, heart disease or enlargement, hernia, absent cremaster reflex, lead in urine, atypical blood-smear pictures, increase of red-blood cells resistance to hypotonic salt solutions, decreased percentage of hemoglobin and weak hand grips.

Diastolic Pressure. This varied from 62 to 112 mm. with 15 cases over 90 mm.; 14 of these higher diastolic pressures occurred in cases with abnormally high systolic pressures.

Pulse Pressures. This varied between 30 and 97 mm. There were 79 between 35 and 60 mm. There were 8 over 60 mm., all occurring with high systolic pressure. There were 13 under 35 mm., all occurring with low systolic pressure.

Systolic Pressure after Exercise. Rose from 1 to 30 mm. in 91 cases; remained the same in 5 cases, and dropped in 4 cases.

Diastolic Pressure after Exercises. Rose a few millimeters in 8 cases; remained the same in 74 cases; dropped a few millimeters in 17 cases. However, there is no apparent relation between these slight variations and the pressures previously noted, nor with any particular group of symptoms.

Of the total of 100 men, 83 were examined in the afternoon, 12 in the forenoon, and 5 in the early evening.

Although blood-pressure determinations of one sitting cannot be given too much reliance, still the fact that in fully one-third of the cases the findings were at or above the upper limit of normality has some significance. This is particularly so when we take into consideration the report of Mr. John A. Runnberg, the statistician of this same union, issued March 1, 1913, from which I quote:

"A recent investigation as to the causes of death of 100 members during the last four years, reveals the fact that the five great

causes of death are organic heart disease, pulmonary tuberculosis, nephritis, pneumonia and accident at work. Almost one-fourth of all deaths are due to some disease of the circulatory system, of which organic heart disease alone exceeds the general death-rate of the city by about 32 per cent. The investigation further shows that the average age at death from any of these five causes is from two to seven years less than the corresponding death-rate in the city at large."

SUMMARY. Of 100 painters examined under favorable conditions: (*a*) Definite symptoms of acute plumbism could not be said to obtain in any case. There were no acute abdominal or nervous cases, none showing erythrocytic basophilia in significant amount (that is nothing approaching 1 per cent. of the total number of red cells). However, 2 cases, gave a positive Liebermann hemolytic resistance test and 2 others exhibited lead in the urine, and there was a suggestion of traces in others. (*b*) Symptoms, signs or after-effects of chronic plumbism of varying degrees, after eliminating other factors, so far as possible, were found in a total of 70 cases. It is not easy to summarize these records, but they fall failry well into the following groups:

Group 1 (history, symptoms, physical signs, tests). Includes 19 men who gave a clear history of previous lead poisoning, 12 of a history suggestive of lead poisoning, 7 were suffering at the time from symptoms clearly indicative of chronic plumbism, and who, in addition, exhibited physical findings and abnormal results in one or more of the tests described above (not including the sodium sulphide test). Average age, 46.16 years, and time at trade 28.15 years. Only 4 were under forty years and 1 over sixty years of age.

Group 2 (history, symptoms, physical signs). Includes 16 men; 7 with a clear history of plumbism and 9 with a suggestive history. All were suffering from symptoms ascribable to chronic plumbism, and were found by physical examination to have systemic diseases ascribable to chronic toxemia. Special tests were negative or borderline only. Average, 34.56 years, and time at trade 16.75 years. Only 3 were over forty years.

Group 3 (history, symptoms, tests). Includes 7 men; 3 with a clear history and 4 with a suggestive history of plumbism, complaining of typical symptoms and responding positively to one or more tests. Physical findings negative or in abeyance. Average age, 40.43 years, and time at trade 25.14 years. Decade distribution uniform.

Group 4 (symptoms, physical signs, tests.) Includes 12 men who had no history of former attacks, but who were at the time suffering from typical symptoms, and who had positive physical findings and responded abnormally to one or more tests. Average age 43 years, and time at trade 23.75 years. Decade distribution uniform.

Group 5 (history, physical signs, tests). Includes 5 men; 2 with a clear and 3 with a suggestive history of lead poisoning; not complaining of ill health, but with physical signs pointing to chronic plumbism and with abnormal response to one or more tests. Only 1 under fifty years (a man aged 40 years). Average age, 51.40 years, and time at trade 32.20 years.

The following 11 cases are less distinctive, but must be looked upon as suspicious:

Group 6 (history, symptoms). Five men whose history was suggestive and who complained of more or less typical symptoms, but physical findings and tests were without material significance.

Group 7 (history, tests). Two men had a history of former attacks and had marked weakness of the wrists but an absence of recent symptoms, also other abnormal physical findings.

Grooup 8 (lead line). Two men showed lead deposits in the gums as the only acceptable manifestation. Alcoholism probable cause of other features.

Group 9 (pyorrhea, weak wrists.) Two men showed pyorrhea and weak wrists only. There was an absence of suggestive history, symptoms, and other features.

With the above groups of workers, age and time at trade have nearly equal curves. Analysis of the four means of arriving at a diagnosis (history, symptoms, physical signs, and special tests) shows:

(*a*) In the younger men (under forty years the tests above described are most apt to fail, while history, symptoms, and certain physical signs are usually present (Group 2).

(*b*) Among middle-aged men (forty to forty-five years) there is a small group (a part of Group 3) which fail to show significant physical signs while the other features are present.

(*c*) A fairly large class (Group 4) composed of men of all ages gave no significant history.

(*d*) Among men over middle age, forty-five years and above, there is a large class (Group 1) showing evidence of every sort indicative of chronic plumbism.

Among the 30 remaining cases were many with suggestive findings, but the preponderance of secondary factors caused them to be eliminated. These cases were as follows:

One each of diabetes, syphilis, tabes (?), Graves' disease (?), hyperchlorhydria, migraine (since childhood in a young man whose blood-pressure was 145), and senility; 6 cases of cardiac or circulatory disease; 8 negatives; and 9 indefinites.

CONCLUSION. Seventy of 100 painters showed evidence of chronic plumbism. The most frequent factors of value in diagnosing chronic plumbism in painters are:

(*a*) Significant past history of certain complaints as noted above.

(*b*) Frequency of certain recent symptoms as noted above.

(*c*) Neuromuscular abnormalities—as tremor, slight incoordinations, abnormal reflexes, weakened hand-grip, and weakened wrists.

(*d*) Circulatory disturbances affecting the blood-pressure, the heart, and the urine.

(*e*) Conditions of the gums—pyorrhea, rarely lead-line.

I desire to acknowledge the valuable suggestions and assistance received from the Director and various members of the staff of the Sprague Memorial Institute; from Dr. Alice Hamilton, and others. I would also state that the coöperation and assistance of the officials, particularly Mr. J. A. Runnberg, and Mr. G. M. Hanson, statistician and secretary respectively of the painter's union from which the men came, deserve mention, while the fact must not be forgotten that every man who was examined volunteered his time and person to promote the undertaking.

FATAL GASTRO-INTESTINAL HEMORRHAGE.

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Sudden gastro-intestinal hemorrhage is fortunately not a common cause of death. Hemorrhage is sometimes the fatal termination of enteric fever and other diseases, but the sudden occurrence of gastric and intestinal hemorrhage with those in the enjoyment of practically good health is one of the most alarming incidents in the work of a surgeon or physician. In presenting the following cases, we have excluded those which were considered due to the commoner causes of hemorrhage, such as ulceration of the stomach or bowel, aneurysms rupturing into the tract, blood disorders, or malignant disease. Neither did we include those fatal cases, in which the clinical signs indicated an unusual etiology, but in which no confirmatory postmortem examination was obtained.

Case I.—A. L., male, aged thirty-three years, was admitted to Dr. Armstrong's service at the Royal Victoria Hospital October 18, 1912. The patient left Toronto on the night of October 17, 1912, perfectly well. After eating a hearty breakfast in Montreal he was suddenly seized with vomiting, and emitted a basinful of

bright red blood. He had to be carried to bed. A second hemorrhage occurred that evening, and he was taken to the Royal Victoria Hospital. An examination of the blood showed it to be normal. The stomach was inspected, but no source of hemorrhage was found; the viscus was full of blood, also the transverse colon. An examination of the stomach mucosa failed to show any erosion or the slightest ulceration, and even after wiping off the mucosa no oozing could be detected at any point.

A postmortem examination was made six hours after death—it was practically one of those negative autopsies in which no demonstrable cause of death could be found. The body was well nourished, of splendid physique, and 165 cm. in length; rigor mortis was present; dorsal lividity absent. Skin was pale; eyes light brown; pupils equal. The chest was bulging. The abdomen was flat. There was a median incision extending from the costal angle downward in the midline 13.5 cm. in length.

There was no abnormality discovered in the circulatory or respiratory systems, excepting signs of obsolescent phthisis in the apices of the lungs.

Digestive System. The esophagus was pale and the epithelium desquamated in places. No varices were found in the esophagus. The stomach was normal in size and contained a small amount of mucoid material and some bright red blood. A posterior gastro-enterostomy wound was present; its edges were a deep purple. The remainder of the gastric mucosa was bright red and contained fluid blood; a few erosions were present, visible only under careful examination, the result apparently of recent operative manipulations. They were inadequate to cause the fatal hemorrhage. The pyloric ring was well-marked, and there was no indication of a recent or chronic gastric ulceration.

The duodenum was 6 c.c. in circumference; it was uniformly congested, and the follicles were enlarged. The contents were blood-stained. There were no signs of duodenal ulcer. The remaining portion of the small intestine showed no ulceration; the contents were composed of brownish clotted blood.

There was no abnormality found in the large bowel, excepting that the contents were intermingled and the bowel distended with tarry blood.

The *liver* weighed 1020 grams, and measured 20 × 15 × 7 c.c. The organ was small, the edges were sharp, and the cut surface was pale. There were several areas in which the connective tissue of the organ appeared increased, but there was no generalized increase. There was one small fibrous nodule in the substance of the liver, about the size of a small marble, which faded into the surrounding tissue.

Microscopically.—The liver showed a few areas of cirrhosis. The portal connective tissue was slightly increased in amount; necrosis

of the liver cells had occurred in a few situations. Focal collections of inflammatory cells were present in the portal connective tissue. The liver cells for the most part stained deeply, but their contour was obscured.

Gall-bladder. The gall-bladder was full of viscid, yellowish-brown bile, the walls were not thickened; there were no hemorrhages.

Pancreas The pancreas measured 16 × 3 × 1.5 c.c. It showed no abnormality.

Spleen. The spleen disclosed no abnormality. It was not increased in size.

Kidneys. The kidneys showed no fibrosis, and no inflammatory cell infiltration when sectioned. No abnormality was observed in the gross specimen.

Adrenals. The adrenals were cavitated.

A feature of interest was the abundance of hemolymph nodes throughout the upper abdomen and along the aorta.

Blood. The blood showed a greatly delayed coagulation time, and an intense polymorphonuclear leukocytosis was found of the adult and multifid type. Juvenile forms were not noted. The red cells showed no particular change. Some films were full of strepto-diplococci. The two psoas muscles were remarkably friable.

The postmortem examination was unable to throw any light upon the causation of the fatal hemorrhage in this case. The only departures from the normal were: in the liver, which showed some slight areas of fibrosis, and some slight mucosal erosions in the stomach.

The possibilities which exist as to the causations were: (1) That the hemorrhage was the result of diffuse oozing from all parts of the gastric mucosa. (2) That it was a case of hemophilia; there is no evidence in the history of the existence of such a condition.

CASE II.—A. L., male, aged fifty years, was admitted to Dr. Martin's service at the Royal Victoria Hospital for dropsy which began one month before admission. One week before he came to the hospital he had had severe abdominal cramps, jaundice, and clay-colored stools. He had been a heavy drinker. He had marked ascites, and over 1400 ounces of straw-colored fluid were withdrawn from his abdomen at different times during his three weeks in the ward. The night following the last withdrawal he vomited some black material, and the next day about ten ounces of clotted blood. The following day he died in syncope.

The autopsy performed by Dr. Gruner disclosed an interesting condition. The stomach was 32 × 25 c.c., and was distended with 680 grams of semisolid blood; no gross source of hemorrhage could be found in the stomach or duodenum, but a few mucosal erosions were present near the cardiac end of the viscus, and the lower third of the esophagus contained a number of dilated and prominent veins, evidently the source of the hemorrhage. Some

tarry blood was found in the small and large bowel. In addition to these findings the liver was markedly cirrhotic. The portal vessels were small, and there was marked proliferation of the bile ducts. There was no bile infiltration observable. A condition of perihepatitis was present. Other findings were an hypertrophied spleen; tubercles over the peritoneum; ascites; chronic interstitial pancreatitis; chronic mixed nephritis; arteriosclerosis.

CASE III.—Boy, aged four and a half years, a patient of Dr. J. J. Gillis, of Merritt, B.C., a former house surgeon at the Royal Victoria Hospital, to whom we are indebted for the clinical notes.

When two and a half years old the boy was treated for an illness resembling typhoid fever and liver trouble in a hospital in Vancouver, B.C. The history is not very definite, but he was ill for six weeks. Save for this illness he has always been a healthy child. On the evening before his sickness he ate a hearty supper, and when getting out of bed the following morning he vomited a large quantity of bright red blood. He was hurried to the hospital, and on the way had several hemorrhages; during the day he had two dark-colored bowel movements. For two days he did very well, but on the third day he had two more hemorrhages, and died. Only a partial autopsy was permitted. When the stomach and duodenum were opened blood was found, but no ulcer nor any enlarged varices. A number of pin-pointed hemorrhagic spots were noticed over the stomach. The stomach and duodenum were sent to one of us for examination, but there was nothing found to account for the source of the hemorrhage.

CASE IV.—M. B., female, aged seventy years, service of Dr. Martin; found in moribund state; no history obtainable; superficial abdominal veins were prominent; marked edema of legs and abdominal wall; ascites; died few hours after admission to Royal Victoria Hospital. Postmortem by Dr. Grunner: Cirrhosis of liver; hemorrhage into the stomach, duodenum, and jejunum; unruptured aortic aneurysm; general arteriosclerosis.

CASE V.—D. McK., male, aged thirty-eight years; service of Dr. Hamilton; marked alcoholic history; brought to outdoor department and was unable to give a coherent account of his illness. Jaundiced; died a few hours after entrance. Postmortem by Dr. Gruner: Fatty liver; enlarged esophageal veins; hemorrhages into the stomach; mitral stenosis; fatty heart; ascites; fibrosis of the spleen.

COMMENTS. The etiology of cases of sudden gastric hemorrhage similar to those we have outlined is not clear in every instance. W. J. Mayo is of the opinion that "where gastric hemorrhage accompanies cirrhosis of the liver, splenic anemia, and disordered blood states it may be attributed to toxic erosions of the gastric mucosa." Although the nature of the toxic process is not well understood, yet evidence is not wanting which indicates that in

a certain number of these cases microörganisms are the causative agent.

The majority of observers are inclined to the view that the gastro-intestinal hemorrhages occurring in the newborn are of toxic origin; thus Litzenberg reported the finding of Friedländer's bacillus from hemorrhagic areas, found in a case of fatal hemorrhage in a child, two days old.

Cases of purpura are of common occurrence; the type associated with Henoch's name is usually characterized by submucous gastro-intestinal hemorrhages, severe abdominal pain, tenderness, and distention; purpura and effusion into the joints are also present. In his original paper on the subject in 1874 he reported four cases, all under fifteen years of age, in which recovery took place after repeated attacks.

Howard, in 1899, expressed the view that organisms of the Bacillus mucosus capsulatus group as well as streptococci were able to induce hemorrhagic septicemia, accompanied by gastro-intestinal hemorrhages, by a degenerating action on the bloodvessels leading to rupture, as well as destruction of the red blood cells themselves.

As is well known, there are many varieties of bacilli loosely classified under the term Bacillus mucosus capsulatus; while their ability to induce hemorrhage may not characterize all, yet it seems to be a quality of some of this group. Howard was able to isolate a variety of the Bacillus mucosus capsulatus in a fatal case of hemorrhagic septicemia which showed cultural peculiarities at variance, with other well-known members of this group.

Hemorrhagic peritonitis has been produced in rabbits, by inoculations with the fluid, from fatal causes of hemorrhagic peritonitis, and different observers have recovered apparently different organisms from such cases.

Jacobson and Post, in drawing attention to hemorrhage from the stomach or intestines, occurring as an initial symptom without pathological disorganization of the mucosa of any kind, recorded several interesting cases. They expressed the view that "certain microörganisms, particularly those possessing the characteristics of the pneumococcus are capable of provoking severe hemorrhage in various parts of the body and that gastric and intestinal hemorrhage can be the first evidence of such a toxemia."

Bolton is of the opinion that a form of erosion of the gastric mucosa which he calls acute gastric ulcer is to be found in many of those obscure cases of severe and fatal hematemesis.

The erosion is often difficult to detect, requiring special mounting in postmortem specimens. It may not be strictly correct to designate these minute erosions by the name of ulcer, and, furthermore, many are inclined to the view that they are of toxic origin.

An interesting collection of cases of fatal gastro-intestinal

hemorrhage was recorded by Preble in 1900; 56 from the literature and 4 which came under his observation. All were found at autopsy to have cirrhosis of the liver. Of these 60 cases the source of the hemorrhage was found in 20 to be from ruptured varices at the lower end of the esophagus. In 15 others the varices were shown, but there was no evidence to the effect that the hemorrhage originated there. In 6 cases the gastro-intestinal mucosa was normal throughout, and no varices were present. The records were not very complete in the remaining cases. In 5 death occurred from the first hemorrhage. Another feature of interest in Preble's collection was the early age of many of the patients. Thus the case reported by Taylor was only five years old. Had had jaundice four months before; liver and spleen were enlarged; later, had ascites and edema; paracentesis. A few days later death after hematemesis. Stomach was full of blood; no erosion or ulceration; liver small; spleen enlarged. The average age of the cases in Preble's collection was close to thirty-five years. Some of his conclusions were that fatal gastro-intestinal hemorrhage is an infrequent but not rare complication of cirrhosis of the liver; that in one-third of the cases the first hemorrhage is fatal, in the other two-thirds the hemorrhages continue at intervals over a period varying from a few months to eleven years; that esophageal varices are present in 80 per cent. of the cases, one-half of which show, macroscopic ruptures; that the cases in which no varices are present are probably due to simultaneous rupture of many capillaries of the gastro-intestinal mucosa; that in only 6 per cent. of the cases which show esophageal varices is the cirrhosis typical, that is, show ascites, enlarged spleen, and subcutaneous abdominal varices.

We are inclined to support the view that the erosions found in the stomach, in some of the fatal cases of hematemesis, are of toxic origin, the nature of which is not definitely known. And it is not improbable that the cirrhosis of the liver found so frequently in these cases is an effect of toxic processes. While there is no definite proof to support the view, yet it is not inconceivable that the infection may have been present in the gastro-intestinal tract for some time, producing effects not severe enough to attract attention. The history of an illness resembling in some features an enteric infection, as well as the varying ages at which the condition may be found, lends some color to this supposition.

The ruptured varices found at the lower end of the esophagus, in cases in which cirrhosis of the liver was also present, explain the source of the hemorrhage in one group of these cases.

The veins of the cardiac end of the stomach are part of the portal circulation, while the esophageal veins are not, there are in this situation connecting links between the two systems, their close proximity to the seat of obstruction aids the formation of

varices; and it is probable that any sudden interference with the circulation might rupture their thin walls. It is possible that interference with pressure, following paracentesis may have been the explanation of the fatal hemorrhage in one of our cases. While this explanation accounts for the hemorrhage in a certain number of cases, yet for the group in which no varices are found, and in which little or no liver cirrhosis is present, another cause must be sought.

An increasing number of cases are being reported in which gastro-intestinal hemorrhage is the most striking feature, and which show at autopsy negative findings; another feature in the majority of these cases is the sudden onset of the hemorrhage.

This group of cases of fatal hematemesis may be attributed to the direct or indirect effect of microörganisms, and it is likely that more attention will be directed to them when our knowledge of the bacteriology of the gastro-intestinal tract is further advanced than at present.

C. A. Ewald thinks that in the female, vicarious menstruation accounts for some cases of severe gastro-intestinal hemorrhage, while other cases may occur from the rupture of diseased arteries in the crisis of tabes. He reports two fatal cases, one in a male, age twenty-four years, the other in a male, aged forty-eight years, in which the autopsy failed to disclose the cause of the hemorrhage.

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THE PROCESS OF BONE REPAIR FOLLOWING TRAUMA.

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The process of the repair of bone after trauma seems to be more or less shrouded in mystery. In reviewing the literature one finds the greatest diversity of opinion. This is largely to be attributed to two facts: (1) that clinicians have reported results frequently

without consulting the microscopic findings, and (2) that satisfactory microscopic examinations are difficult because of the injury incurred by the soft parts while the bone is undergoing decalcification. Some authors invest the periosteum with bone-reproducing qualities, while others claim that it is nothing but a limiting membrane.

In the embryo there are two types of primary ossification, intramembranous and intracartilaginous.

INTRAMEMBRANOUS OSSIFICATION. The basis for development is embryonal connective tissue or mesenchyme. At certain points these embryonal connective-tissue bundles become impreganted with calcium salts, the cells in each of these areas increase in number, some of them becoming more or less round or oval, with distinct nuclei and a considerable amount of cytoplasm, and arrange themselves in single, fairly regular rows along the bundles of calcified fibers. These differentiated cells are known as osteogenetic cells or osteoblasts. Under the influence of the osteoblasts a thin layer of calcium salts is deposited between the osteoblasts and the calcified fibers forming true bone. Successive layers of calcium salts are laid down, enclosing some of the osteoblasts, which then become bone cells. The spaces in which the bone cells lie are called lacunæ.

INTRACARTILAGINOUS OSSIFICATION. In this type of ossification the bone is preformed from hyaline cartilage, which is also derived from embryonal connective tissue. Around this cartilage is a fibrous connective-tissue membrane called the perichondrium. This membrane gradually fades on the one side into cartilage and on the other into the surrounding connective tissue. There is no sharp dividing line. During the early stage, calcium salts are deposited in the matrix of the cartilage, forming an "ossification centre." Later small bloodvessels push their way in from the perichondrium of the new diaphysis, carrying with them some of the embryonal connective tissue. These ingrowths of bloodvessels and connective tissue are called periosteal buds. The septa between the cartilage cells break down, forming large spaces into which the periosteal buds grow. Many of the connective-tissue cells are transformed into osteoblasts, and with the fibers and bloodvessels constitute osteogenetic tissue. This process continues until the primary spongy bone is formed, this being later destroyed by osteoclasts, with a subsequent formation of compact bone.

It is evident from this brief *resume*, that bone in the embryo is formed by a metaplasia from the connective tissue, accompanied by a deposition of calcium salts. Of interest in this connection is the work of Gideon Wells, who has shown that if cartilage is transplanted into the omentum it has a greater power of absorbing calcium from the blood than any other tissue similarly placed.

THEORIES IN REGARD TO BONE REPAIR. 1. *Periosteum the Main Agent in Repair.* This has been recently the most generally

accepted theory. The adherents of this theory consider that the periosteum is a specialized tissue for the formation of new bone, and that bone deprived of its periosteum will eventually die. Much experimental work has been done along these lines. Numerous investigators have transplanted periosteum and observed new growth of bone. MacEwen has offered the criticism that in removing the periosteum a layer of bone cells, osteoblasts, are transplanted also. If a piece of the periosteum, to be transplanted, were saved for microscopic examination this question could be satisfactorily solved. Morpugo demonstrated that the periosteum of a corpse would reproduce new bone when implanted after one hundred and sixty-eight hours. Murphy thinks that if periosteum be transplanted in the same individual, especially if he be young, it will form a lasting bone deposit; but if transplanted into another individual, it rarely produces bone. He, however, states that bone transplanted with or without its periosteum into fat or muscle tissue eventually dies. MacWilliams, in a paper read before the American Medical Association, states that periosteum is necessary for the life of bone transplants, unless the transplants are very small, in which case they grow and unite without periosteal aid. He has demonstrated in his experimental work that large bone fragments transplanted into the soft parts will live if the periosteum be attached, but that they are almost constantly absorbed when transplanted without the periosteum.

2. *Periosteum not a Bone-forming Organ.* MacEwen considers the periosteum to be merely a limiting membrane without osteogenetic functions. He has performed numerous experiments which seem very convincing, although it is frequently difficult to understand his deductions. He has, for instance, removed about 1 cm. of the radius, scraped off the periosteum, and cut the piece removed into small fragments, which were reinserted between the cut ends of the radius. Eleven weeks later the animal was killed and the leg examined. To quote from MacEwen: "Small diaphyseal grafts, when placed in a gap in the continuity of bone, show active proliferation from the whole circumference, each piece being an ossifying centre from which osseous tissue is thrown out sufficient to fill the gap between the various fragments and to unite them together along the two ends of the divided bone."

MacEwen and MacWilliams have both shown that small fragments of bone transplanted into the soft parts will unite and form definite bone, although MacEwen has not allowed time enough to see if the bone would eventually be absorbed.

In transplanting sections of the diaphysis, most authors are united in thinking that the transplanted piece dies, but that union occurs by new bone growing in from the shaft of the host, and also by new bone forming in the Haversian canals and medulla of the transplanted piece.

Barth can see degeneration in the nuclei of the transplanted fragment in one week; in young animals he sees small groups of bone cells until the twenty-second day.

Axhausen has transplanted joints and bones into soft parts, and finds three stages in the transplanted piece. (1) the nuclei take a normal stain; (2) the nuclei become crumpled and distorted; (3) the nuclei disappear and the bone becomes homogenous.

On the other hand, Takata finds that isolated bone fragments are surrounded by irregularly lying, dentated, relatively large cells that closely resemble osteoblasts. These cells are not separated from the surrounding connective tissue, and they lie without any sharp differentiation. The connective-tissue cells become gradually larger as they approach the bone. He considers these fragments to be living bone.

Of great interest is the formation of bone in arteries, new-growths, etc. Bunting, Harvey, Wells, and others have described the formation of true bone in arteries. In Bunting's case there was a formation of bone in a sclerotic aorta. This tissue had a definite lamellar structure with Haversian canals, and a narrow cavity, containing the normal cellular elements. He made a careful histological study, and his conclusions were as follows: "Bone in arteries may be desposited in two ways; either by the conversion of connective tissue into a callous or osteoid tissue, with subsequent conversion into bone and at times with the formation of cartilage, or by the resorption of calcified tissue by vessels and osteoblastic membrane, derived by metaplasia from the connective-tissue cells accompanying the vessel."

Wells believes the reason bone is so rarely deposited in veins is that the excess of carbon dioxide in the venous blood keeps the calcium in solution.

Harvey gives the following theories for the formation of bone in arteries: (1) wandering osteoblasts; (2) metaplasia of connective tissue; (3) metaplasia of mesothelium of blood capillaries. He produced new bone in the aorta of rabbits by painting the adventitia with 3 per cent. solution of silver nitrate, or 2 per cent. solution of copper sulphate. He killed them after various lengths of time, varying from one hundred and ten to one hundred and eighty-six days, and found calcium plaques along the inner edge of the media. On sectioning these plaques he found definite lamellar bone, with Haversian canals, lacunæ, and red marrow cells.

Liek, Poscharisky, Sacerdoti, and Frattin have tied off in rabbits the renal vessels on one side. In from sixteen days to two months the animals were killed. True bone was found adjacent to the calcium deposits in the necrotic connective tissue of the kidney; this was accompanied by a growth of granulation tissue inward from the capsule. Here also was definite lamellar bone.

The writer's work was undertaken to attempt to learn the method

of repair in bone cavities. To accomplish this, Dr. Clarke, director of the surgical research laboratory of Columbia University, suggested making simple cavities in the diaphysis of the humerus in dogs. An effort was made to secure a cavity in which absolute hemostasis occurred, and therefore a dead space. The humerus was exposed, usually by a median incision, the periosteum was removed for a distance of at least 3 cm. in length and for almost the entire circumference of the bone. A rectangular piece, 1 x 0.6 cm., extending into the medullary canal, was removed from the median surface of the diaphysis, and the medullary cavity was thoroughly curetted and packed until hemostasis occurred. Realizing that this hemostasis was only temporary, and that oozing probably occurred from the medullary cavity after suturing the muscles over it, various experiments were tried: (1) the cavity was packed and then filled with hot sterile oil and the wound closed; (2) the cavity was packed with gauze, which was removed in twenty-four hours; (3) the cavity was packed with gauze sterilized in oil, which was removed twenty-four hours later (the purpose of this was to prevent the gauze adhering to the sides of the bone cavity and the subsequent oozing upon its removal); (4) both ends of the cavity were filled with Morehof's bone wax; this caused very good hemostasis, and was used in the largest number of experiments.

In one case a sac was made of the peritoneum covering the appendix. The peritoneum was stripped off and a purse-string suture applied around the opening of the peritoneum; the sac was then filled with salt solution and placed in the bone cavity, completely filling it. The idea was to prevent the cavity from filling with blood clot, and with the hope that the sac would be eventually absorbed. Unfortunately this dog received a gas bacillus infection and died in forty-eight hours.

After varying lengths of time the dogs were killed and the legs hardened in formalin. The gross appearance was then noted. Longitudinal or cross-sections were made. After decalcifying they were sectioned and examined microscopically. It has been a difficult thing to sufficiently decalcify the bone without destroying the soft tissue.

Results. Thirty-eight dogs have been operated upon as described above. Of this number, 4 died of acute infection, 4 sustained fractures following operation, and 6 died of either distemper or lobar pneumonia before a satisfactory length of time had elapsed. The remaining dogs were killed at varying lengths of time, ranging from thirty to one hundred and ninety days. A certain definite type of repair occurred in most of these cases. On cutting down upon the humerus a cavity containing a serosanguinous fluid was entered. The base of this cavity was bare bone of the diaphysis, while the periphery consisted of a flat connective-tissue layer that was continuous with the overlying muscles. These cavities varied from 2

to 5 cm. in length, and in some cases extended around almost the entire circumference of the bone. In the bare bone at the base of this sac was found the former bone cavity extending into the medullary canal. Extending upward from the bottom of the cavity was a pyramidal mass of tissue which microscopically resemble granulation tissue. On microscopic examination this tissue was found to contain a ground-work of granulation tissue, with deposits of calcium salts arranged around the perivascular areas.

In a few cases a definite connective-tissue layer, continuous with the periosteum and adherent to the surrounding structure, has grown over the bone and the cavity has been repaired under this.

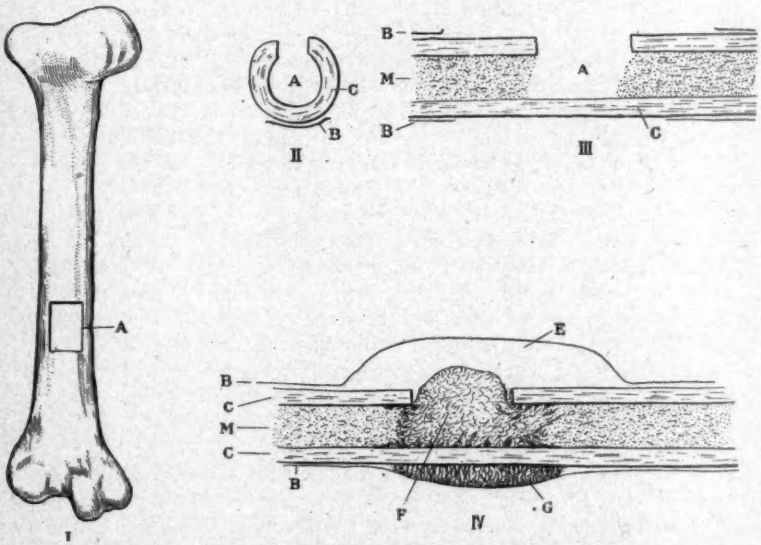

FIG. 1.—Schematic drawings. *I*, cavity in shaft; *II*, transverse section through bone and cavity; *III*, longitudinal section; *IV*, manner of repair of bone cavity. *A*, cavity; *B*, periosteum; *C*, shaft; *E*, cavity under periosteum filled with serosanguineous fluid; *F*, new-forming bone; *G*, bone forming under periosteum; *M*, medullary cavity.

The four cases of fracture were sectioned and studied. Here there was seen a gradual transition of connective tissue into bone It was impossible to make out any definite periosteum.

In giving detailed accounts of experiments only those are given where it has been possible to get good photomicrographs. Those not mentioned have all been examined microscopically, and all show a similar process of repair to those given in detail. It seemed wise to omit giving their histories in detail on account of taking up too much space

Dog No. 362. Surgical Research Series, 1912–1913. Experiment No. 21. Surgical Pathology, No. 2066. Operation, May 27. Death, due to pneumonia, June 8. Duration, twelve days. Median incision, 6 cm. long, over left upper foreleg. Humerus exposed. Periosteum removed for a distance of 3.5 cm. A rectangular piece of bone, 0.8 x 1 cm., was removed from the shaft. This incision extended into the medullary canal, which was curetted and packed for several minutes. Upon removal of the packing, good hemostasis was observed. The muscles were sutured over the defect in the shaft, and the skin was closed with continuous silk.

FIG. 2.—Surgical pathology, No. 2066. Longitudinal section through one-half of cavity. Duration, twelve days. *A*, edge of bone cavity; *B*, new forming bone; *C*, blood clot.

Autopsy. Lobar pneumonia of right upper lobes. Incision wound on leg perfectly healed. Leg hardened in formalin. Upon cutting down on the humerus a small sac, about 2 cm. long by 1.5 cm. wide, is opened. The base of this sac is the humerus and the apex consists of a smooth fibrous tissue membrane apparently continuous with the overlying muscles. This sac contains a sero-

sanguinous fluid. In the humerus at the base of this sac is the aperture in the shaft, which is filled with blood clot.

Microscopic Examination (Figs. 1 to 3). A longitudinal section was made through the humerus. The bone was decalcified with phloroglucin and nitric acid solution. Plate I shows a schematic drawing of the operation and longitudinal sections taken for microscopic examination. The periosteum does not approach the aperture in the shaft for at least a distance of 1 cm. in all directions. Growing up from the base of the medullary canal and from its upper limits is seen a granulation tissue staining a deep blue. This tissue is made up of fibroblasts and other connective-tissue cells. One

FIG. 3.—High power of part of Fig. 2. A new-forming bone, stellate-shaped cells; *B*, areolar connective tissue.

sees a net-work of tissue taking a purple stain which, under high power, is seen to be bone. One is impressed with the idea that calcium salts have been laid down upon ordinary granulation tissue in the perivascular areas; that is, in the areas farthest from the bloodvessels. This is an early formation of new bone.

Dog No. 127. Surgical Research Series, 1912–1913. Experiment No. 29. Surgical Pathology, No. 2237. Operation, December 3, 1912. Died December 19, of pneumonia. Duration, fifteen days. Operative procedure similar to Pathology No. 2066. Healing of operative wound *per primam*. Longitudinal sections made in routine manner. Upon gross inspection the periosteum found

separated from the bone about 0.5 cm. on all sides of aperture in humerus. This bone cavity is seen filled with blood clot.

Microscopic Examination (Fig. 4). The centre of the cavity is seen to be filled with blood clot, and fine interlacing strands of new bone are being formed from the connective tissue. Under high power of the new bone one sees numerous round cells, with dark staining eccentric nuclei. It is possible that these cells are either converting the earlier bone into a denser bone, or they may be phagocytes.

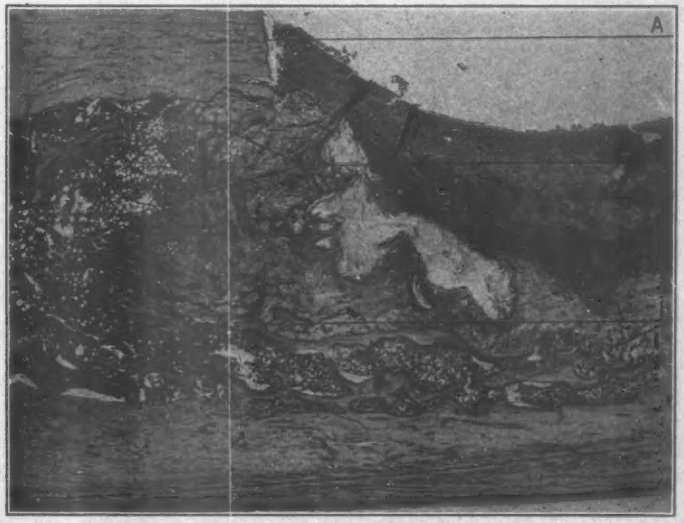

FIG. 4.—Surgical pathology, No. 2237. One-half bone cavity. Duration, fifteen days. *A*, edge of bone cavity; *B*, new bone; *C*, blood clot.

Dog No. 108. Surgical Research Series, 1911–1912. Experiment No. 4. Surgical Pathology, No. 1882. Operation, January 5, 1912. Died of pneumonia February 14, 1912. Duration, twenty-four days. Routine operation.

Autopsy. Lobar pneumonia. Operative wound healed *per primam*. Upon cutting down upon the humerus a sac containing a serosanguinous fluid was opened. This fluid, upon microscopic examination, contains numerous erythrocytes, polymorphonuclear leukocytes, and lymphocytes. The base of this sac is bare bone; in the centre is the aperture in the humerus. The apex of the sac is a smooth, connective-tissue membrane continuous with the overlying muscles. The periosteum is well separated from the bone cavity. The centre of this aperture is filled with a growth of new tissue resembling granulation tissue in appearance; on palpating

this with a needle it is hard and gritty. On longitudinal section this tissue filling the bone cavity is seen to be an early formation of new bone.

Microscopic Examination (Figs. 5 and 6). This bone-granulation tissue arises from the base of the cavity; it has a honey-combed appearance, the lighter staining areas consisting of bloodvessels and connective-tissue stroma, while the darker stained areas are

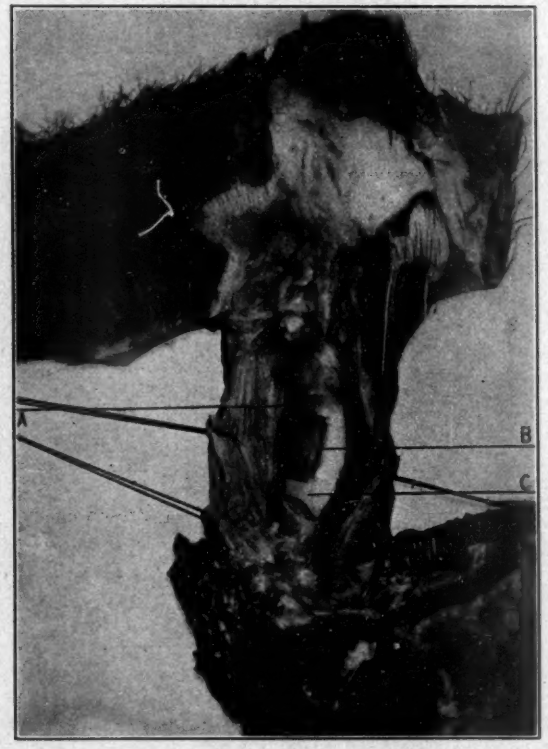

FIG. 5.—Surgical pathology, No. 1882. *A*, edge of periosteum; *B*, new bone filling cavity; *C*, bare bone.

newly forming bone. Here under high power one cannot see that any specific cell forms this bone; it appears rather that calcium salts have been deposited in the perivascular areas upon connective tissue.

Dog No. 361. Surgical Research Series, 1911–1912. Experiment No. 20. Surgical Pathology, No. 2147. Operation, May 27, 1912. Killed October 15, 1912. Duration, 141 days. Piece,

1 x 0.5 cm., removed from lateral surface of left humerus; cavity curetted thoroughly; medullary canal at both ends filled with bone wax. Excellent hemostasis. Muscles and skin sutured in usual manner.

Autopsy. Only slight linear operative scar visible; on palpation the bone feels smooth; no depression or nodules can be felt. On cutting down upon the bone a cavity, 5.5 cm. long by 1.5 cm. wide, is opened; it extends from immediately above the condyle

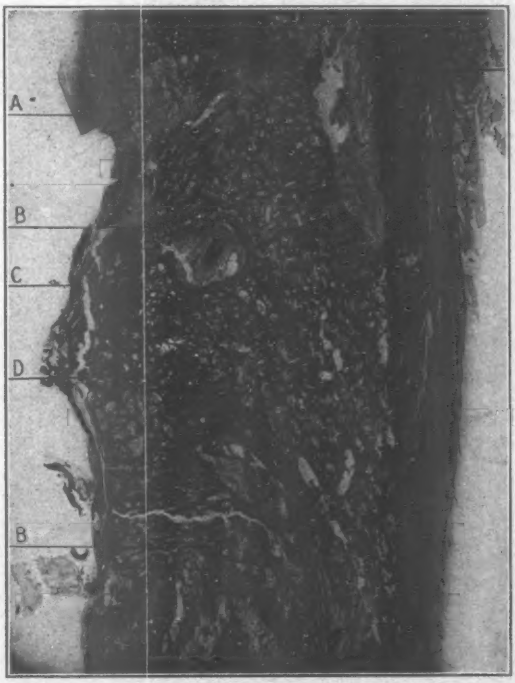

FIG. 6.—Low power. Longitudinal section of Fig. 5. *A*, edge of bone cavity, living bone; *B*, new bone; *C*, connective tissue; *D*, bloodvessels and areolar tissue.

to 1 cm. below the greater trochanter. This cavity contains a small amount of serosanguinous fluid; its base is formed by bare bone. The centre surface is a fibrous tissue membrane adherent to and apparently continuous with the adjacent muscles. On the humerus about 0.5 cm. below the upper limit of this sac is a small oval depression in the bone; it measures about 4 mm. in diameter and 2 mm. in depth. At the bottom of this depression is a small shot-like piece of bone which has the appearance of a sequestrum; *x*-rays,

however, show there is no sequestrum, but there is a definite rarefaction of the bone at this location.

Microscopic Examination (Figs. 7 and 8). The bone which bridges over the aperture is much more cancellous than normal; the Haversian canals occur more frequently, and are larger. The bone cells are present and stain with hemotoxylin and eosin. In the small piece at the bottom of the depression the cells appear

FIG. 7.—Surgical pathology, No. 2147. Duration, one hundred and forty-one days. *A*, bone cavity; *B*, bare bone; *C*, periosteum.

shrunken and stain poorly, but it has not the appearance of dead bone, as the cells and Haversian canal systems can be clearly made out. Immediately below this bridge, in the medullary canal, is a cavity, which before decalcification was filled with bone wax and blood-clot; around this is a thin capsule of new bone. In this case the bone has reformed, with the periosteum stripped off from the bone for a distance of 5 cm. This bone is living bone; the process of repair is probably a later stage to the previous cases.

Dog No. 392. Surgical Research Series, 1911–1912. Experiment No. 24. Surgical Pathology, No. 2148. Operation, June 17, 1912. Killed October 15, 1912. Duration, one hundred and twenty days. A piece, 1 x 0.8 cm., removed from the median surface of right humerus; the medullary canal was thoroughly curetted and packed; after removing the packing good hemostasis was observed. Muscles and skin sutured in usual manner.

Autopsy. Only a linear scar visible; humerus feels smooth. On cutting down upon the bone a sac similar to Pathology No. 2147 is opened. It is difficult to observe where the aperture was in the humerus; there is a very slight depression in the bone.

FIG. 8.—Low power of Fig. 7. *A*, new-forming bone; *B*, new-forming bone, showing enlarged Haversian canals; *C*, base of cavity *A* in Fig. 7.

Microscopic Examination (Figs. 9 and 10). The most noticable thing in the new bone is the direction of the Haversian canals. Instead of running parallel to the surface they lie perpendicular to it, so that it is easy to determine the junction of old and new bone. In the medullary cavity numerous strands of bone are seen running toward the new bone. In comparing this section with Pathological No. 1882 it would seem that this is a later stage of a similar

type of repair; the direction of the Haversian canals indicate that it originated from the tissue of the medullary canal.

Dog No. 325. Surgical Research Series 1911–1912. Pathological, No. 2180. Operation, May 6, 1912. Died December 7, 1912. Duration, one hundred and ninety days. Cavity made in humerus in usual manner, good hemostasis. Wound healed *per primam*. Animal in good shape; killed by chloroform.

FIG. 9.—Surgical pathology, No. 2148. Duration, one hundred and twenty days. *A*, depression at situation of former bone cavity; *B*, bare bone; *C*, periosteum.

Autopsy. On cutting down upon humerus it is difficult to find the site of the former operation, only a slight depression being visible. The bone is completely covered with fibrous tissue continuous with periosteum and adherent to the overlying muscles.

Microscopic Examination (Fig. 11). The aperture in the shaft is almost entirely filled with new bone. In this portion, however, the Haversian canals run perpendicular to the surface rather than horizontal to it. Spicules of new bone are seen traversing through the tissue of the medullary canal immediately beneath the former aperture.

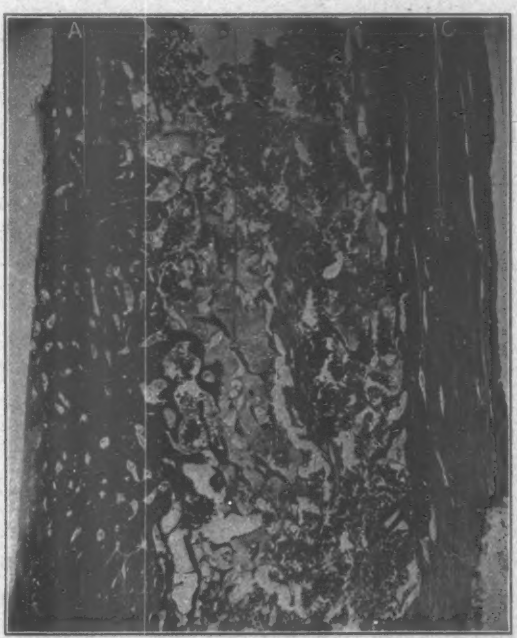

FIG. 10.—Longitudinal section of Fig. 9, under low power. *A*, edge of former cavity—Haversian canals run perpendicular to surface; *B*, bone strands; *C*, bone at bottom of cavity.

Dog No. 88. Surgical Research Series, 1911–1912. Experiment No. 2. Surgical Pathology, No. 1907. Operation, January 12, 1912. Cavity in humerus by usual method. On January 24, the dog jumped off a chair and fractured the foreleg. Animal killed with chloroform February 21. Duration following fracture is twenty-eight days.

Autopsy. Wound in leg healed; there is non-union, with considerable over-riding of the fragments. There is considerable thickening about the ends of the bone. On cutting down upon the humerus one finds marked callous formation.

Microscopic Examination (Fig. 12). There is new bone proliferating from the outer surface of the ends of the fractured bone; no definite periosteum can be made out. Under high power

one finds a definite metaplasia from connective tissue to fibrocartilage, from connective tissue to bone, and from fibrocartilage to bone. In the areas of new-bone formation one finds first a layer of fibrous connective tissue that gradually changes into newly forming bone. There are all stages of metaplasia between the cartilage and the bone cells. The nuclei becomes irregular, often stellate, the deep blue of the capsule gradually fades and eventually disappears, and the cell takes on all the characteristics of the bone cell.

FIG. 11.—Surgical pathology, No. 2180, under low power. Duration, one hundred and ninety days. *A*, section of former bone cavity—Haversian canals run perpendicular to surface; *B*, junction of old and new bone; *C*, bone spicules in medullary cavity; *D*, bare bone.

Dog No. 251. Surgical Research Series, 1911–1912. Experiment No. 12. Surgical Pathology, No. 1997. Operation, March 25, 1912. Routine operation. On April 1 the dog jumped off a table and broke his leg. April 8 an attempt was made to get some callous cells to grow *in vitro*, and the leg was amputated at the fracture line. The transplants did not show any growth; a small

spicule of bone with surrounding callous was taken for microscopic section.

Microscopic Examination (Fig. 13). Under low power the specimen looks like a lace curtain, the darker perivascular areas being the calcium deposits while the lighter areas are granulation tissue and bloodvessels. This arrangement is clearly shown under high power.

FIG. 12.—Surgical pathology, No. 1907, under high power. Transition of connective tissue into fibrocartilage. *A*, fibrous connective tissue; *B*, fibrocartilage.

Dog No. 117. Surgical Research Series, 1912–1913. Experiment No. 28. Surgical Pathology, No. 2250. Operation, November 25, 1912. Cavity made in usual manner. Wound healed by first intention. On December 10 the dog jumped off a chair and fractured his humerus. Animal killed with chloroform on December 27. Duration, seventeen days.

Autopsy. There is considerable callous formation around the broken ends. No union has occurred, as there is a definite false point of motion, with over-riding of the fragments. Leg hardened

in formalin. Cross-sections taken through broken ends of the bone, including callus and surrounding connective tissue.

Microscopic Examination (Fig. 14). Around the periphery of the shaft there is proliferating new-bone formation. It is impossible to make out periosteum, as it fuses with the general connective-tissue infiltration. Surrounding the callus and new-bone formation is a fibrous tissue stroma. The loose ends of the bone are covered with tissue that resembles cartilage.

FIG. 13.—High power of surgical pathology, No. 1997. *A*, callous (new-forming bone); *B*, bloodvessels.

Beginning at the periphery there is a gradual transition from the surrounding connective tissue into fibrocartilage. Beyond the cartilage one sees strands of new-bone formation; there are places in this new bone where there are islands of cartilage cells; the cartilage cells become gradually smaller; their nuclei becomes irregular or stellate in shape, and their capsules gradually lose their blue stain and disappear, until there seems to be no definite dividing line between the cartilage and bone cells.

Dog No. 248. Surgical Research Series, 1912–1913. Experiment No. 36. Surgical Pathology, No. 2394. Operation, February 11, 1913. Upon attempting to make a cavity in the usual manner the leg was fractured. A Lane plate was applied, with fair approximation of the two ends; and wound was sutured and the leg put up in plaster of Paris.

FIG. 14.—Surgical pathology, No. 2250. Repair of fracture. *A*, connective tissue; *B*, transition of connective tissue to osteogenetic cells; *C*, new bone; *D*, cartilage cells embedded in bone.

March 4 the cast was removed; wound healed. There was, however, no union, so the dog was killed with chloroform. Duration since fracture, twenty-two days.

Autopsy. The ends of the bone are thickened and club-shaped, and have considerable callus around them. Longitudinal sections made through the ends of the bone.

Microscopic Examination (Fig. 15). Here under high power one sees again gradations between connective tissue, cartilage, and bone.

CONCLUSIONS. In this series of experiments two types of repair of the bone have been observed:

1. Where the periosteum has been well stripped off the bone for a distance of several centimeters it is separated from it by serosanguinous fluid. Here the bone has apparently been repaired from the medullary cavity by a framework of connective tissue, upon which calcium salts have been deposited, forming osteoid tissue; there has also been a reparative process from the connective tissue of the Haversian canals at the sides of the bone incision.

FIG. 15.—Surgical pathology, No. 2394. Repair of fracture, under high power. *A*, cartilage; *B*, bone.

2. Where the bone has repaired under a definite fibrous connective-tissue capsule, which is continuous with periosteum and also adherent to the surrounding muscles. This connective tissue is apparently not different from other connective tissue, except that in immediate approximation to the newly forming bone there is a single layer of cells which are larger in shape and have nuclei that take a heavy stain. In places there is a metaplasia from the connective-tissue cells to these osteogenetic cells.

In the process of repair in fractures by the output of callus there is a metaplasia from connective tissue which seems to arise from the surrounding tissues rather than being a direct continuation of the

periosteum. There is also a direct metaplasia from a tissue closely resembling fibrocartilage into young bone.

In attempting to draw clinical deductions from these experiments in regard to transplantation of bone, it is reasonable to assume that the periosteum acts as a limiting membrane to the bone, tends to conserve its shape, and to furnish its blood-supply. If the periosteum is stripped from the bone of the transplanted part, numerous thrombi will occur, where the vessels enter the diaphysis; but if the periosteum is left attached, the blood-supply will probably be more quickly established through the vessels of the periosteum.

If small pieces of bone are transplanted, it is obvious that Haversian canals must be cut in many directions, thus allowing easy ingress to the newly forming bloodvessels. The fragments also must receive a good blood-supply from the entire periphery. They grow in this case without the aid of periosteum.

I wish to extend my thanks to Drs. Clarke, Auchincloss, and Prime for many kind suggestions and valuable advice, and to Dr. McWhorter and Mr. Agnew for making the photomicrographs.

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DIABETES MELLITUS AND ITS DIFFERENTIATION FROM ALIMENTARY GLYCOSURIA.

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Ten years ago anyone whose urine reduced Fehling's copper solution on boiling was considered to be suffering from diabetes mellitus, and the patient was directed by the attending physician to regulate his earthly affairs and prepare for death at any moment. So many of these individuals were seen to outlive all expectations, and finally to show no sugar whatever in their urines, that it led to a more thorough study and understanding of the condition. To the work of von Noorden,[1] with his oatmeal diet, more than to anyone else is due the credit of first establishing a scientific therapy for such; while Opie,[2] Mohr,[3] von Mering and Minkowski,[4] Lusk,[5] and others have given us a deeper insight into the pathology of the disease. Opie[6] has shown that in the majority of cases there is a degeneration of the cells in the islands of Langerhans in the pancreas, with atrophy of same. While there is no doubt that pathological changes in the pancreas will cause glycosuria, the writer has seen fatal cases of diabetes in which no pathological changes could be demonstrated in this organ, but in which they seemed to be limited to the liver, while other cases are reported in which no lesions whatever could be demonstrated. We must, therefore, content ourselves with a meager knowledge of the pathology of this disease and turn to physiology to explain many of the phenomena observed.

The various changes through which the carbohydrates pass before final utilization by the tissues as fuel is shown in the accompanying table.

Von Noorden[7] believes that the pancreas through its harmone inhibits the liver in its normal tendency to part with its glycogen, and that failure of this action results in a hyperglycemia from overproduction of glucose. He does not think there is any lack of ability in the tissues to utilize the glucose in the blood. However, the recent experiments of Knowlton and Starling[8] would tend to disprove this latter idea, and show that the pancreas while it does

[1] Metabolism and Practical Medicine, Chicago Med. Book Co., 1907.
[2] Jour. Exper. Med., 1901, v, 527; Johns Hopkins Hosp. Bull., 1901, xii, 263; Disease of the Pancreas, Philadelphia, 1910.
[3] Sammlung klin. Abhandlungs über Path. u. Ther. der Stoffwechsel u. Ernahrungsstorungen-H, 4, Aug. Hirschwald, Berlin, 1904.
[4] Arch. f. exper. Path. u. Pharm., 1890, xxvi, 371.
[5] Science of Nutrition, Philadelphia, 1909.
[6] Loc. cit.
[7] New Aspects of Diabetes Mellitus, New York, 1912.
[8] Jour. Phys., No. 3, xlv, 162.

have an influence on the glycogenic function of the liver most certainly has a decided influence on the utilization of glucose by the tissues. The main point to bear in mind from a clinical standpoint is that whenever the normal glucose content of the blood (that is, 0.09 per cent.) is exceeded, the kidneys will excrete the excess and glucose will appear in the urine. It has been thoroughly accepted that the pancreas secretes a harmone which is absorbed by the blood and in some way presides over the glycogenic function of the liver.

Food substance.	In alimentary canal split up into:	Absorbed by portal system and transformed by liver into:	Stored up in muscles as:	Burned up by tissues into:	Remarks.
Saccharose, $C_{12}H_{22}O_{11}$.	Dextrose, $C_6H_{12}O_6$, and Levulose, $C_6H_{12}O_6$.	Glycogen, $C_6H_{10}O_5$. Glycogen.	Glycogen. Glycogen.	CO_2 and H_2O glycuronic acid. CO_2 and H_2O glycuronic acid.	Dextrose and levulose are excreted by the kidneys if not utilised by the tissues.
Starch, $C_6H_{10}O_5$.	Dextrose.	Glycogen.	Glycogen.	CO_2 and H_2O, glycuronic acid.	
Maltose, $C_{12}H_{22}O_{11}$.	Dextrose, $C_6H_{12}O_6$.	Glycogen.	Glycogen.	CO_2 and H_2O, glycuronic acid.	Excess maltose excreted by kidneys.
Lactose, $C_{12}H_{22}O_{11}$.	Dextrose and galactose.	Glycogen.	Glycogen.	CO_2 and H_2O.	When liver is deranged, galactose appears in urine.
Cellulose, $C_6H_{10}O_5$.	Very little if any effect in human.				
Proteids.	Peptones, amino-acids, xanthine bases. Ammonia. Toxic amines from intestinal putrefaction.	Serum, albumin, and globulin. Urea. Non-toxic compounds.	Syntonin, creatin, etc. Creatin. Creatin.	Urea, uric acid, glycocol, and dextrose.	If liver function is deranged, have lowered akalinity of blood.
Fats.	Absorbed through lacteals and into general circulation through the liver. Do not pass through the liver. Incomplete combustion results in diacetic acid.				

Anything affecting the cycle between the liver and the pancreas will result in glycosuria, or anything causing a rapid rise of the dextrose in the general circulation will cause a glycosuria, maltosuria, or galactosuria, depending in great part upon the particular carbohydrate eaten. Patients partaking of large amounts of milk often show a reduction of Fehling's solution, not because they have a true diabetes, but because their normal liver function has been overtaxed, with consequent chronic passive congestion of this organ, so that it is unable to transform into glycogen the galactose formed from the lactose in the milk. A liter (one quart) of milk yields about 48 grams of lactose, which is split up into 24 grams of

dextrose and 24 grams of galactose. The latter is differentiated from the former by its failure to ferment with a pure culture of Saccharomyces Ludwigii and its action on polarized light, while both reduce Fehling's solution. In hepatic insufficiency the liver is able to transform the dextrose into glycogen, but has lost this power for galactose. So constantly is this the case that the ingestion of 40 grams of lactose on an empty stomach, with a subsequent determination of the amount of galactose in the urine for four to six hours is universally adopted in the German and Austrian clinics as a test for liver function. This is an example of what one would regard as an "alimentary glycosuria," although glucose is not the sugar present.

Another type of alimentary glycosuria is exemplified by a case recently referred to me as a case of diabetes mellitus:

CASE I.—R. P., wholesale grocer, had suffered some prostatic trouble, and in the routine examination of his urine, by Drs. Hume and Logan, a heavy reduction of Fehling's solution was obtained, and he was referred to me. There was no thirst, no loss of weight, nor nervous manifestations of diabetes, and his urine was inactive to polarized light, yielding 7 per cent. calculated dextrose by reduction. Urine fermented by yeast. There was no diacetic acid or acetone. Specific gravity, 1.028, with a heavy reaction for indican. He gave a history of eating large amounts of sugar during the day, as he made a practice of grabbing a handful every time he passed the open sugar barrel in his warehouse. His liver dulness was increased to 14 cm., but otherwise all his organs were normal. On account of the failure in action to polarized light, it was evident that there was not a simple glycosuria, and inasmuch as the reduction ceased on the second day after his arrival in New Orleans, I concluded that it was a glycolevulosuria, due to the rapid absorption of the dextrose and levulose formed from the cane-sugar, with insufficient action of the liver and prompt excretion of both saccharides by the kidneys, together with some glycuronic acid.

He was put upon a low proteid diet to rest up the liver. No sugar was allowed, but glutinous substances and vegetables were given, while his liver function was stimulated by an initial calomel purge and a two weeks' stay at one of the spring resorts, whose water is rich in phosphate and sulphate of soda. On his return his liver dulness had diminished to 8 cm., there was no reduction with Fehling's solution, and after taking 100 grams of lactose on an empty stomach no galactose could be detected in the urine.

He went home happy in the thought that he had been cured of diabetes, but, fortunately, he never had a true diabetes, but had a simple alimentary glycosuria from insufficient liver action and an overindulgence in cane-sugar. Such cases as this von Noorden classes as prediabetic, and yet "they may go for a lifetime and never develop a true diabetes."

In diabetes mellitus there is a failure of the entire body to utilize not only the dextrose of the circulating blood, but there is a predilection for fat and proteid as fuel in preference to carbohydrate, with subsequent formation of beta-oxybutyric acid, acetone, diacetic acid, etc., from incomplete combustion of these foodstuffs. That incomplete combustion of proteids, or their excessive putrefaction in the intestines, can cause an acid condition in the blood identical with that seen in diabetic coma, I am firmly convinced, although I am not in accord with modern text-books on this point. Diacetic acid, acetone, and beta-oxybutyric acid are not particularly toxic, and I have seen fatal cases of diabetic coma whose urines just previous to death showed very little of these sustances, but which were loaded with the products of intestinal putrefaction. Most practitioners make the mistake of considering the carbohydrate metabolism and not payng any attention to the proteid metabolism.

The following case shows the importance of a consideration of the latter:

CASE II.—L. N., white male, aged fifty years, manager of a saw mill, was referred to me by Dr. Picard on May 20, 1912, complaining of drowsiness, occasional headaches, with excessive thirst and ravenous appetite. Other than an attack of lobar pneumonia, twelve years before, he had never had a day's illness until 1905, when he consulted Dr. Picard for retention of urine, which was very abundant. Dr. Picard informs me that at this time he had vague abdominal pains and crampy pains in the limbs, and that his urine showed 2– per cent. of glucose. He had been getting along very well until ten days previous to his visit to me, when he had a sudden attack of nausea and vomiting, succeeded by a constant drowsiness and inability to remain awake sufficiently to attend to his business. He had been losing weight steadily for the past four years, but during the past ten days he had lost nearly twenty pounds.

Examination revealed a robust, ruddy individual, with all organs apparently normal, with the exception of a hypertrophied heart and a general emphysema. There was only moderate peripheral arteriosclerosis, and examination of the fundi showed both disks normal, with no pathological changes in the retina. Examination of his urine showed: specific gravity, 1.040; acid; 1.5 per cent. glucose by polariscope; large amount of albumin; great excess of indican and diacetic acid; negative urobilinogen; a few hyaline casts.

He was sent to Touro Infirmary, and was put upon Vichy and large amounts of bicarbonate of soda. A purgative of calomel, phenolphthalein, and rhubarb was administered, and a reduction in proteid food, with increase of carbohydrate food, instituted at once.

The following table shows his diet and the results of same:

Date.	C.c. urine passed in 24 hours.	Grams glucose in 24 hours.	Total calories.	Carbohydrate calories.	Calories lost in urine.	Per cent. calories lost in urine.	Weight, lbs.	Indican.	Remarks.
May 22	1280	28.1	1215	600	115.4	9.5	154	++++	Full proteid diet.
May 23	Lost	...	3175	1025	...	...	...	++	Full carbohydrate diet
May 24	2050	44.5	3825	1550	221.4	5.7	...	+	Oatmeal and corn-bread.
May 25	1570	35.8	3125	1440	146.7	4.5	...	0	Oatmeal and corn-bread.
May 26	1650	33.0	2450	775	135.3	5.5	155	0	Oatmeal and corn-bread.
May 27	1600	39.3	2500	1250	143.4	5.5	...	0	Macaroni.
May 28	2040	36.1	2525	1125	148.0	5.8	156	0	Oatmeal.
May 29	1650	25.1	2475	1150	103.2	4.1	...	+	Macaroni.
May 30	1760	35.2	2675	1075	144.3	5.4	...	0	Rice and potatoes.
May 31	1700	41.8	2675	975	172.0	6.4	...	0	Rice and potatoes.
June 1	1760	37.4	3475	1325	153.6	4.4	...	0	Oatmeal.
June 2	1170	37.1	4200	2850	152.3	3.6	159	0	Oatmeal and corn-bread.

He left the infirmary in two weeks, a changed man; his mind perfectly clear, no headaches, and an increase in weight of five pounds. I have heard from him at intervals of from three to four weeks, and he has continued to improve on a liberal carbohydrate diet. His urine contains 3 per cent. of sugar still, but there is no albumin and no diacetic acid, and he is to all intents and purposes a well man. He is able to assimilate oatmeal, corn-bread, and macaroni, as well as large amounts of fruit, but he cannot metabolize saccharose, rice, and potatoes.

It must be borne in mind that approximately 50 per cent. of the proteid molecule is transformed into glucose in the body metabolism, and that for every 1 gram of nitrogen in the urine, 5 grams of glucose are either burned up by the tissues or excreted by the kidneys, so that in endeavoring to rid the urine of sugar one must take this fact into account. It has been my experience, (and upon this fact also depends the good results of the von Noorden "Hafer Kur") that the excretion of sugar may increase for a short while after giving carbohydrates, but even during this greater excretion of glucose a greater percentage is utilized by the tissues. This is well exemplified in the diet table accompanying Case II.

It is not the purpose of this paper to consider all of the many points in physiological chemistry involved in a consideration of diabetes, but merely to call attention again to the fact generally accepted that complete withdrawal of carbohydrate food from a diabetic for a long period of time, invariably results in an acidemia, commonly spoken of as diabetic coma, in which beta-oxybutyric acid, diacetic acid, and acetone are usually found in the urine. It is also well to again mention that in the metabolism of proteids,

approximately 50 per cent. of the proteid molecule is split off as a carbohydrate radical, and that this accounts for the continued presence of dextrose in the urine even after complete withdrawal of all carbohydrate food. Dextrose itself is relatively non-poisonous in comparison to the other cleavage products of proteids, and before outlining a diet a consideration of the cleavage products of proteids should be considered, even more than those of carbohydrates.

The amount of glucose excreted by the kidneys is of far less importance than a consideration of the amount of diacetic acid, beta-oxybutyric acid, acetone, and indican. In referring to the tabulated chart of Case II, it will be noticed that on days of carbohydrate feeding, while he excreted a larger amount of glucose, the percentage of wasted calories compared to that ingested was progressively less, while he gained steadily in weight and all symptoms disappeared.

In the treatment of diabetes, drugs or proprietary medicine are of no benefit, if we are to judge by published reports, and the treatment resolves itself into a regulation of the patient's diet and personal hygiene, so as to avoid acidemia, which, however, when present, can be relieved by drug therapy. In overcoming the tendency to intestinal toxemia the writer has experienced good results from the administration of massive doses of cultures of the Bacillus bulgaricus, but the number of cases are as yet too few to draw any conclusions. Since Knowlton and Starling's[9] article, we have administered 10 to 20 grains of an active extract of pancreas, every four hours on an empty stomach, with decided and rapid reduction, and even complete absence of glucose in the urine in two cases of diabetes, while in two others there was apparently no effect.[10]

Therapy along this line should, theoretically, yield good results, but the difficulty of obtaining absorption of the pancreatic harmone before it can be destroyed by the gastric juice will always remain a difficult problem. It is to be hoped that in the near future this harmone can be isolated and preserved in such a manner that it can be administered hypodermically, when the ideal drug for the disease will have been found. Until then, strict regulation of the diet will have to be relied upon, and for successful results one must consider the proteid metabolism, as well as the carbohydrate metabolism, and be ever mindful of the physiology underlying the condition.

[9] Loc. cit.

[10] Eustis. Acidosis, New Orleans Med. and Surg. Jour., September, 1913, vol. lxvi.

CHLOROMA, WITH REPORT OF A CASE OF THE MYELOID VARIETY.

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The uncertainty that exists in the classification of a group of diseases of which the above title represents one, is such as to demand that all these be published, with the hope of ultimate clarification of our knowledge.

In the following report, one of us (F. X. W.) is responsible for the clinical observations, and the other for the pathological study, which was undertaken while the latter was a member of the department of pathology, of the Northwestern University Medical School. It is our desire, therefore, to express our obligations to this department, and especially to Professor F. R. Zeit, who furnished valuable suggestions.

Synopsis. *Clinical.* Five-year-old white male; entire illness three months; proptosis and tumors about face; general glandular hyperplasia; gingivitis and necrotic pharyngitis, blood; moderate anemia; leukocytes, 9000 to 12,000, 80 per cent. of which were mononuclear, 4 per cent. of total were myelocytes, and a smaller number were myeloblasts; spleen and liver markedly enlarged.

Pathological. Chloroma deposits found in following locations: orbits, in frontal bones (sinuses, etc.), in temporal bone, on external surface of parietal bones, attached to cerebral and spinal dura mater, kidney, liver, and posterior surface of sternum. Eosinophilic mononuclear cells were found in some of the chloroma masses.

Clinical Data in Detail. C. M. R., white, male, aged five years, was brought to Wesley Hospital July 10, 1906. The child having been cared for in a public institution, the exact time of onset is unknown, but probably was six or eight weeks before admission to the hospital, the child at this time having just recovered from pneumonia. The first indication of illness was swelling between the eyes and at the angles of the jaw. There has been a gradual increase in the size of the swellings and a gradually increasing depression of spirits. Sleep has been troubled, and the facial expression has indicated some pain. Ten days before admission, stomatitis with bleeding gums was noted.

Previous Illness. Uneventful attacks of measles and chickenpox. Pneumonia just before onset of present trouble.

Family History. Mother is in an insane asylum on account of dementia following a puerperal infection. Parental lues denied.

EXAMINATION, July 31. *General.* Nutrition somewhat poor. Extremities slightly bluish. Eyelids dark bluish red, firm; pit slightly on pressure; otherwise no edema, except over forehead, where it is slight. Lips are a trifle cyanotic. Subcutaneous veins are prominent over both temporal regions, and extend forward onto brow.

FIG. 1.—Chloroma. Shows tumor of glabella and spongy gums.

Head. There is a large protuberance between the eyes and extending to the brow. This tumor seems to push apart the two halves of the face. The distance from one inner canthus to the other is 3 cm. The mass is quite hard, but softer than bone. There is a similar hard, dome-shaped mass 5.5 cm. in diameter in the right temporal region. This mass is smooth, not nodular, and harder than the one on the face. There is a similar swelling about 2.5 to 3 cm. in diameter in the left temporal region. The eyes are prominent, and seem to bulge from their sockets. Conjunctivæ (bulbar and palpebral) much injected. Eyes water. Pupils moderately dilated and react normally. No extrinsic paralysis. There is a thin frothy discharge from both nostrils. Mucous membrane of left naris injected. Slight abrasion at mucocutaneous junction. Mouth exhibits extensive inflammation of both gums, with ulceration. Tendency to bleeding. Foul odor. Teeth slightly loosened, but no evidence of decay. Tongue slightly coated. Pharynx injected and edematous. Tonsils not visible.

Facies. Pathetic. Voice thick. Marked coryza.

Neck. Lymphatic glands beneath right ear enlarged. They are freely movable and somewhat sensitive. Considerable number of pea-sized glands beneath the jaw. Anterior and posterior cervical glands enlarged and hard. Same true of axillary and inguinal groups. Epitrochlear glands are the size of small shot.

Thorax. Negative.

Abdomen. Slightly prominent. Lower pole of spleen on the level of the umbilicus, and its right border extends to the rectus muscle. Notch distinctly palpable.

Liver. Extends 7 cm. below costal arch.

Progress of the Disease. The symptoms, including the facial distortion, proptosis, conjunctival injection, became gradually more pronounced. The child became thinner, paler, more peevish and irritable, and complained of pains in the head. Pupils became slightly unequal. During the last week of life, fever was almost constantly present, being nearly always over 101°. Although the roots of the teeth became bare, the latter were not markedly loose. The pharynx presented a dark, gangrenous appearance; several gangrenous masses of almost unendurable odor were expelled during the act of coughing on the day before death. Manipulation of the mouth caused free hemorrhage. During the last week of life there was a noticeable diminution in size of all the swellings about the head. The mass between the eyes, in addition to diminishing in size, became somewhat softer. The face, however, has an appearance similar to that seen three or four weeks previously, although eyes project to less extent. (The diminution in the size of the swellings, etc., occurred during the administration of potassium iodide.) The child grew steadily worse, but was able to sit up and even to walk up to the last day.

August 14, 1906, the patient died quietly and without warning.

Blood Examination. (The following represents a synopsis of fourteen examinations made between July 12, 1906, and August 11, 1906, inclusive:)

Erythrocytes	3,300,000 to 2,400,000
Leukocytes	9,400 to 12,000
Hemoglobin	50 per cent. to 60 per cent.

Differential count of leukocytes:

Polymorphonuclear neutrophiles	18.0 per cent.
Lymphocytes	60.0 "
Large mononuclears	16.0 "
Polymorphonuclear eosinophiles	.7 "
Myelocytes	4.0 "
Myeloblasts	1.3 "

The myelocytes have a diameter of about 15μ. The cells, few in number, called myeloblasts by some writers, measure about 18μ. They represent an early or embryonic stage of the myelocyte.

The erythrocytes exhibit some lack of uniformity in size, there being a fair number of microcytes and megalocytes. No polychromatophilia. No nucleated reds. In general they are well stained; a few cells, however, were pale.

Pathological Findings. In the following notes the microscopic findings accompany the postmortem description of each organ. The microscopic description of the chloroma mass in the orbit, the bone-marrow, etc., is reserved for the end of this section.

The autopsy was held in the morgue of Wesley Hospital, a few hours after death.

The body is that of a male child, 102 cm. in length. There is a swelling in the frontonasal region circular in outline and measuring 3.5 to 4 cm. in diameter; it is firmly adherent to the bone. A mass of lymph glands was found in the inframandibular region of each side. The chain of posterior cervical glands enlarged. On vertex of head is seen a mass similar to one in frontonasal region, but slightly smaller.

Head. On removing the scalp, there is seen on right and left temporal regions and extending to coronal suture a greenish substance not readily removed. The internal aspect of the calvarium exhibits in the frontal and parietal regions a similar material. The bone is rough and shows spicules. Both retrobulbar spaces are filled with a soft, greenish material. The same material is found in the left temporal bone (petrous portion), but not in right, and also in the frontal sinuses. The dura mater exhibits on its outer aspect the same greenish material, which at one place has broken through so as to appear on the inner surface of the membrane. Between the spinal dura and the vertebræ is found a greenish substance similar to that found in the head. At the level of the seventh cervical vertebra it forms a tumor-like mass the size of a navy bean.

Brain. Weighs 1152 gm. Externally and on section negative.

Spinal Cord. Grossly and microscopically no changes.

Larynx. The upper part of the larynx shows necrosis, as does also the epiglottis and the fauces. The nasopharynx exhibits necrotic masses, which on microscopic section show complete necrosis of the mucosa and submucosa and of some of the layers of striped muscle. Between the bundles of muscle fibers and even between the individual fibers are seen mononuclear cells, some of which are ordinary lymphocytes, but many of them are larger cells supplied with large, pale nuclei.

Thorax. Attached to the internal aspect of the sternum at the junction of the manubrium with the gladiolus is what appears to be a lymph gland. On section this material has a microscopic structure, almost identical with the orbital tumor, although a moderate number of spindle cells is seen. The right pleural cavity exhibits a few easily torn adhesions.

Lungs. The left lung weighs 162 gm. Floats high in water. Pale in color. Numerous split-pea-size purple areas firm to touch. The right lung weighs 176 gm. Also floats high. Areas as in other lung, containing little or no air. Fibrous adhesions obliterate the fissure between the upper and middle lobes. Cutting into the anterior part of the lung, pus is found in the bronchi, also what appears to be inflammatory tissue is seen. The small, airless areas in each lung exhibit microscopically the following: Some of the alveoli are filled with serum, but for the greater part they are filled completely with cells without being accompanied by an appreciable amount of fibrin. In some areas there are a few polymorphonuclear cells; the vast majority of the cells, however, are mononuclear. Some of these (in some areas a considerable number) resemble the lymphocyte; however, in the majority of areas examined the preponderance of cells is represented by a cell with a chromatin-poor nucleus. Also, this same infiltrate is seen in the alveolar walls. In many places, where the infiltrate is marked, it is impossible to distinguish the alveolar walls. The anterior portion of the right lung mentioned above as containing pus, etc., exhibits microscopically the following: A massive infiltration is found, the greater part being found in the wall of and surrounding a large bronchiole, part of whose epithelial lining is missing. In the infiltrate are found a moderate number of thin-walled vessels. Although the infiltrate contains a considerable number of cells, with poorly stained nuclei, a much greater proportion (than in small areas mentioned above) are seen approaching the adult type of cell, especially the lymphocyte. The polymorphonuclear leukocyte is present, but not in great numbers. A few eosinophilic mononuclear and polymorphonuclear cells are seen. We interpret the above findings to indicate an invasion of the lungs by the same cells as are found elsewhere. There has been some inflammatory reaction to this. The pus in the bronchiole is due either to breaking down and infection of a chloroma infiltrate (as seen in the pharynx), or possibly to the occlusion of the bronchiole followed by infection, due to the pressure of the infiltrate.

Heart. Weighs 94 gm. Myocardium somewhat pale. Valves normal. Microscopically, no marked changes.

Lymph Glands. The lymph glands at the bifurcation of the trachea are markedly enlarged; some of them are as large as hickory nuts. On section they are pale and show no caseation.

Abdomen. Cavity is dry.

Liver. Greatly enlarged and extends in right mammary line 12 cm. below the costal arch, and in median line 14 cm. below the ensiform. Weighs 947 gm. Dimensions: 19 x 16 x 11 x 7 x 4.5 cm. The enlargement of the organ affects mainly the right lobe. At the hilum several large glands are found. The organ on section presents a pale appearance and the markings are less distinct than

normal. Microscopically, in the portal territories are found moderately extensive infiltrations of cells of which each has a single nucleus. These nuclei in some cases are deeply stained, and in others have a vesicular appearance. These cells correspond fairly well in size to those seen in the retrobulbar masses. Similar cells are seen between the columns of liver cells. Otherwise the organ appears normal.

Spleen. The spleen is greatly enlarged, extending 7 cm. below the costal arch in the anterior axillary line. Weight is 231 gm., and dimensions 14 x 8.5 x 4 cm. Near upper pole, fibrous tags are seen. The color is uniformly pale and the markings are less distinct than normal. On microscopic examination the Malpighian bodies are much less distinct than normal. The cells of the pulp are mononuclear, and vary in size from the dimensions of the ordinary lymphocyte up to diameters of 10μ or more. In general the larger cells have nuclei which are less deeply stained. A few cells having a diameter of about 20μ, and containing 3 to 5 nuclei, are found. A considerable number of mononuclear cells are found with eosinophilic granules. These cells measure about 10μ in diameter and their nuclei take a moderately deep stain.

Kidneys. The right kidney weighs 72 gm.; appears pale. Capsule strips readily. Markings are fairly distinct. The ratio of cortex to medulla is 1:2. The cortex contains a white nodule as large as a pinhead. The left kidney weighs 75 gm. The cortex contains a greenish-white mass surrounded by a hyperemic zone. This mass, measuring about 1 cm. in diameter, appears on section somewhat wedge-shaped, with the base at the surface of the organ; otherwise the description of the right kidney applies. Microscopically, the kidneys show the following: The epithelium of the convoluted tubules seem slightly lower than normal. Some of the nuclei of these cells take the stain poorly and in some the nuclei cannot be found. The capsule of Bowman exhibits some distention; however, no evidence of abnormal contents is seen. The pinhead-sized nodule mentioned in the right kidney and the larger wedge-shaped area in the left have a similar structure, except that the latter has a somewhat looser texture, and one description, therefore, will apply to both. These masses, microscopically, do not have the sharp line of demarcation found in the ordinary neoplasm. The cells are supported by a delicate fibrous network. An occasional thin-walled vessel is seen in the midst of the cells, which are practically all mononuclear, only a few having two or three nuclei. No granules were seen. The diameters of the cells run up to 13 to 15μ, more of the cells in the nodule of the right kidney attaining this size than in the nodule of the left. The nuclei are in part poor in chromatin; other cells, however, exhibit nuclei with good staining powers. No cells resembling the ordinary small lymphocyte were seen.

The *mesenteric* and *lumbar glands* were all enlarged, reaching the size of split peas.

Pancreas. The *pancreas* weighs 40 gm., and shows no changes.

Stomach and *Intestines* show no change.

Urinary bladder, no change.

Left adrenal, no changes (right not found).

Marrow. The *marrow* of the right femur has a greenish-reddish appearance.

MICROSCOPIC EXAMINATION OF MASSES IN ORBIT, ETC. *Retrobulbar tumor.* This is a mass of cells supported by a fine network of fibrous tissue. A moderate number of thin-walled vessels is seen. The cells are fairly large in type, about one-half of them measuring 10 to 12μ in diameter. No polymorphonuclear leukocytes were found, the cells being all mononuclear, with the exception of a moderate number containing each two or three nuclei, possibly the result of subdivision. There is a moderate number of cells whose nuclei take the stain somewhat deeply, resembling lymphocytes. The majority of the cells, however, have rather large, more or less poorly stained nuclei, which are always surrounded by fair amounts of protoplasm, although the nucleus occupies more than one-half the diameter of the cell. The nuclei are round or oval. A very few eosiniphilic mononuclears are seen.

The *tumor* in the *spinal canal* in general is the same as structure just described, there being, however, a slightly larger number of eosinophilic mononuclear cells.

The *mass* in *glabella* (the structure was decalcified) corresponds to the two tissues above described, containing, however, as does the mass from the spinal canal, a larger number of eosinophilic mononuclear cells than does that from the orbit.

The *tumor* from the *dura mater* has the same structure as the orbital mass.

Smears from *bone-marrow* (only the hematoxylin-eosin specimens were of value). Practically all the cells are mononuclear, only an occasional polymorphonuclear being seen. They range in size up to 18μ, the large type predominating. The nuclei occupy the larger part of the cells, the protoplasm not being made out distinctly in most cases. The nuclei in appearance are midway between the embryonic and adult types. An occasional mononuclear cell with eosinophilic granules is seen. In the paraffin sections of the bone-marrow the cells correspond in a general way to those just described, although a large proportion of what appears to be small lymphocytes is seen. Also the nuclei throughout are more deeply stained.

PATHOLOGICAL DIAGNOSIS. Myeloid chloroma with deposits in the orbits, sinuses of the frontal bone, petrous portion of the temporal bone, external aspect of the parietal bones, on cerebral and spinal dura, in pharynx, lungs, kidneys, spleen, and liver.

Bone-marrow changes. Chronic diffuse nephritis of the parenchymatous type (moderate degree).

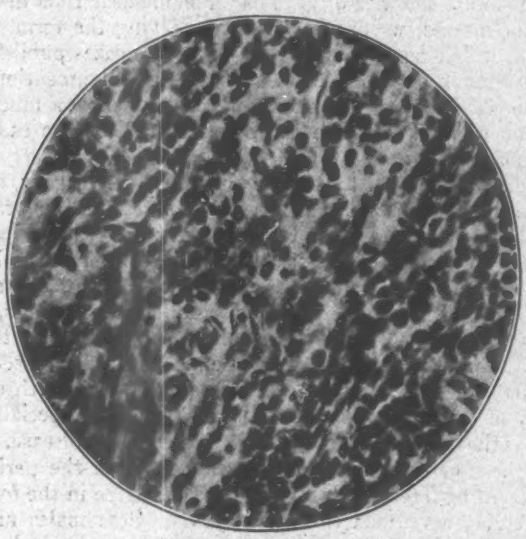

FIG. 2.—Chloroma. Tumor mass from orbit. × 350.

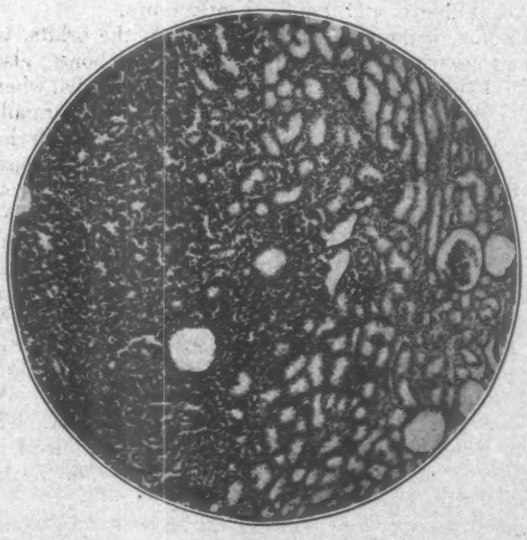

FIG. 3.—Chloroma. Infiltration of right kidney. × 60.

That we are dealing with a case of chloroma, there can be no doubt; and inasmuch as some myelocytes were found in the blood, and a moderate number of granular mononuclear cells in some of the tumor masses, we are justified in applying the term myeloid chloroma, which represents, judging from the cases published, the more uncommon form of the disease. It should be mentioned here that other cases of myeloid chloroma reported show a much larger proportion of myelocytes in the blood than does the case under consideration.

That chloroma is a disease of the blood-making organs, and not, as at one time supposed, a neoplasm ("green cancer") is practically undisputed. It would seem to fit in best with acute leukemia. Treadgold, in a masterful article, endeavors to point out, between the two conditions, certain differences which impress one as being differences of degree rather than of kind. Some authors, among whom are Treadgold and Dock and Warthin, state that the chloroma, compared with acute leukemia, exhibits greater malignancy; not so much, however, in its rapidity of growth as in its tendency of the cells to invade surrounding tissue, especially bone; and this is the reason that we observe, in the former disease, the cells leaving the bone-marrow and appearing beneath the periosteum. As suggested by Treadgold, the two diseases agree in the following: Age: average, seventeen to twenty years. Sex: males more frequently afflicted. Symptomatology: weakness, marked anemia, hemorrhagic tendency, splenic and glandular enlargements, deposits in the liver, kidneys, and less frequently lungs.

In chloroma, deposits occur commonly in the orbits, temporal region, and elsewhere in relation to the cranial bones; also in the prevertebral tissue, skin, and other locations (organs) where tissue analogous to that found in chloroma does not normally exist. However, non-chloromatous growths sometimes occur in these locations in association with lymphatic leukemia. In chloroma the cells are, on the whole, larger and possess more perinuclear protoplasm, not alone in the blood and bone-marrow, but also in the tissues. Treadgold believes, therefore, that the greater pathological malignancy may be accounted for by the additional quantity of protoplasm in the morbific cells increasing their ameboid powers.

Are we able to make a clinical diagnosis of chloroma? When we consider that at least two cases have been described (Birk, Leber), typical pictures of the disease without the lesions having a green color, we must answer this question in the negative. We must content ourselves with a diagnosis of acute leukemia. The more important clinical manifestation, aside from the blood changes, is the presence of tumor masses about the bones of the face; but this sign sometimes fails.

But sometimes we have evidence during life of invasion of the cranial bones without visible tumors being present. For example,

in Gumbel's case the patient, on account of involvement of the petrous portion of the temporal bone, suffered from disturbances of hearing. In the cases of v. Recklinghausen, Sternberg, Schmorl, Waldstein, Hitschmann, Türk, and Lenhdorff no evidence is furnished in the reports of invasion of the cranial bones. However, in a case of acute leukemia if we find evidence of masses in the orbits (proptosis), tumors about the glabella or in the temporal regions, we may reasonably expect to find these masses of a green color when the autopsy is performed.

But why be so concerned about a hair-splitting diagnosis? The more literature one reads concerning this class of diseases the more is he confused with the various terms used. It is quite well settled that acute lymphatic leukemia originates in the bone-marrow. The same is true of even chronic lymphatic leukemia, with few, if any, exceptions. The disease under consideration has the same point of origin. Therefore, when we compare chloroma, which is essentially acute, with other acute leukemias, one is not able at all times to draw hard and fast lines, especially if we ignore the green color, this being, of course, an autopsy finding. However, the tumors about the head, being the common thing in chloroma, and of infrequent occurrence in the other leukemias, are always indicative of an unusual type of leukemia. Summing up the whole situation, it seems that for an absolute diagnosis of chloroma we must depend upon the presence of the green color of the lesions at autopsy. The source of the color has always been an interesting question. Practically all authors agree that this disappears a short time after the body is opened. In our case we have an exception, inasmuch as the color persisted in preserving fluid (Kaiserling). In fact, even after a lapse of more than four and one-half years the masses in the dura mater, although somewhat darker in shade than at the time of the autopsy, were still distinctly greenish in tint. Ayers makes the following statement in regard to the specimen from his case: "On having placed the tumor in alcohol, the color disappeared entirely within twelve hours. On the other hand, the specimen kept within a tightly corked bottle, still retains the greenish color; in fact, the color has become even more intense." It is quite well settled that the color is not due to foreign pigment, such as iron. The consensus of opinion seems to indicate that it is something inherent in the cells of the tumor masses much the same as we have, in plants, green protoplasm (chlorophyl). Treadgold says in regard to the peculiar color: "We have already seen that abnormal myelocytes and myeloblasts are the pathogenic cells in chloroma and that green lesions never exist in pseudoleukemia, lymphosarcoma, and acute lymphatic leukemia. Possibly a degeneration of the granules or perigranular protoplasm of these cells, or an abortive attempt to form granules is the real

source of the color, aided by the broken-down products of hemoglobin."

Blood Findings in Chloroma. The blood shows an anemia evidenced by a diminution in the number of erythrocytes and in the percentage of hemoglobin. Of course, the severity of the anemia in a given case will become more and more accentuated as the patient approaches his fatal termination. In the case of Pope and Reynolds, the erythrocytes numbered only 900,000 and the hemoglobin 25 per cent. In Türk's case the red cells went as low as 583,000, and the hemoglobin at one time 19 per cent. and later 14 per cent.

Sometimes nucleated erythrocytes are found; Sternberg reports not only normoblasts, but also some megaloblasts.

The leukocytes are usually increased in number, and may show a count of 300,000 or more. However, in the case of Lehndorff, published in 1910, the count was only 5100; in our case 12,000 was the highest count, while in Bramwell's case 13,000 was never exceeded. The number of leukocytes, therefore, is not of paramount importance. The significant finding is the presence of cells of embryonic type, cells from the bone-marrow that represent the forerunner of the myelocyte. These cells are sometimes called marrow cells ("Mark Zellen" of the Germans). Others use the term "myeloblast." The same cell is found, of course, in the blood of acute leukemia. In Buchanan's *The Blood in Health and Disease* an excellent chart is given showing the derivation of the leukocytes. In this the cell under consideration is called a non-granular myelocyte. It is a large, non-granular, mononuclear cell, with a nucleus more or less embryonic in type (pale) and occupying the larger part of the cell. In our case the embryonic type of cell forms a much smaller percentage, and the lymphocytes a larger percentage than is true of most cases of chloroma.

Two Varieties of Chloroma. This refers to the lymphoid and the myeloid types. The myeloid variety is supposed to bear to splenomyelogenous leukemia, the same relation as does the lymphoid type to lymphatic leukemia. Paulicek and Wutscher reported a case in which the patient, aged twenty-six years, was suffering from what was apparently an ordinary splenomyelogenous leukemia. After receiving *x*-ray treatment for one month, he was discharged from the hospital as improved. Five months later he returned, and his autopsy, at the end of a two months' stay in the hospital, showed chloroma. Roman furnished a list of the myeloid variety of chloroma previously reported. As previously mentioned, we believe that our case belongs in this group. In this type one should find myelocytes in the blood. At least some of the cases have exhibited in the chloroma masses, granular mononuclear cells, which of course will have to be grouped with the myelocytes. The myelocytes in the the blood may reach a high

percentage. Pope and Reynolds report 32 per cent. and Türk 47 per cent. It will be recalled that in the specimens from our case, we found cells with eosinophilic granules, as reported also in the case of Klein and Steinhaus.

COURSE. The disease runs a course lasting usually a few months (two to four). Some patients have lasted less than eight weeks. Others have run a longer course: Horing's case (seven months.) Huber's (over one year), Schmidt's (fifteen months), Dock's (one year). The disease is essentially fatal.

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A NEW METHOD OF GASTRIC TESTING, WITH A DESCRIPTION OF A METHOD FOR THE FRACTIONAL TESTING OF THE GASTRIC JUICE.

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While the passage of the stomach tube in the great majority of cases is an easy matter, it is questionable whether routine examina-

tion by this instrument is desirable. The average individual is willing to submit to almost any procedure when the condition of his digestion is such as to call for relief, but will hardly be in sympathy with such methods when his digestion is only temporarily deranged. Furthermore, while there are some authors, like Bourget, who consider that the stomach-tube has almost no contra-indications, there are others who find many conditions which might militate against its use. Needless to say, there are many occasions when we desire a sample of or information about the gastric juice without inconveniencing the patient, and it is toward the solution of this problem that I wish to report simple direct methods for the estimation of gastric juice. For years physicians have sought for some other method of examining the gastric contents than by the ordinary stomach-tube and the possible methods at our command may be enumerated as follows:

DIRECT METHODS. The most important of these is the Einhorn bucket. While I have not had any direct experience with this instrument, I have experimented with a bucket of similar shape and dimensions. It is true that it represents a possible method of examining the gastric contents, but it is by no means free from objections. Its construction is such as to permit the passage of pharyngeal and esophageal secretions in the superior orifice of the capsule, and even though precaution be taken to thoroughly gargle the throat, this by no means obviates the esophageal mucus which is called forth by the passage of the instrument.

The same thing may be said regarding the sponge and string method of Spallazani and Edinger. It is almost impossible to pull either the sponge or bucket up without encountering pharyngeal or esophageal secretions.

The use of the Dunham thread test and the recent gastrognost of Freidrick's is likewise open to the same objections, and I question whether the mottled staining of the latter, which its author details as characteristic of chronic gastritis, may not be due to its passage through the esophagus.

INDIRECT METHODS. It has been proposed to give bicarbonate and auscult for effervescence. Anyone who has had experience with this method knows how inconstant and unsatisfactory it is. It represents one of those methods which theoretically should be good, but which fail in practice. In many cases in which the bolus of food is more or less firm and free hydrochloric acid is undoubtedly present, but few crepitations are heard. To my mind its only value is in hypersecretion, where a continued shower of fine rales might suggest the condition. The use of the Leon Meunier ether capsule gives very irregular results, as I have frequently had occasion to witness.

I therefore conceived the idea of using a simple capsule which could be easily swallowed and withdrawn at any given interval.

In this capsule substances were placed capable of indicating the condition of the gastric juice. There was some difficulty in having such a capsule cut, but it was finally made of hard steel, plated with silver. Fig. 1 shows such an instrument in different sizes. It consists of two parts: the head perforated to permit the passage

FIG. 1.—Enlarged view of capsule.

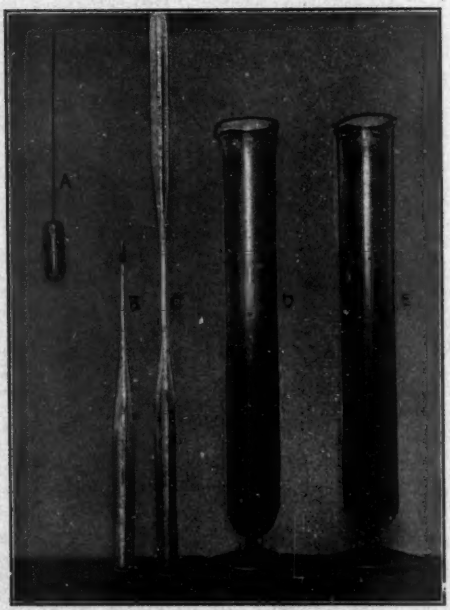

FIG. 2.—Material for preparing capsule.

of a small silk thread, and supplied with a screw thread, by which it is attached to the body. This is likewise perforated and slotted to permit of the greatest possible ingress of liquid.

In experimenting with indicators, I found the best possible base was one of agar-agar, which recommends itself, owing to its form

and consistence as well as its known refractivity to digestion. It is a very workable medium, and can be prepared in tubes like the various bacteriological media. It is best to use a 2.5 per cent. solution, as the addition of various coloring matters will soften it somewhat. Various substances were tried: Congo red, phenolphthalein diamidoazobenzol, litmus, of these only the first two gave appropriate media. I found, for instance, that while it was possible to prepare an excellent preparation of Congo red by adding a 1 per cent. aqueous solution of Congo red to the agar-agar jelly after it has cooled to 40°, the same solution added to hot agar-agar results in a precipitation of the dye, which is of little value. Usually it is well to see that the jelly is distinctly alkaline by adding a few drops of $\frac{n}{10}$ NaOH. When these precautions are observed, a clear red jelly is obtained. Phenolphthalein being soluble in

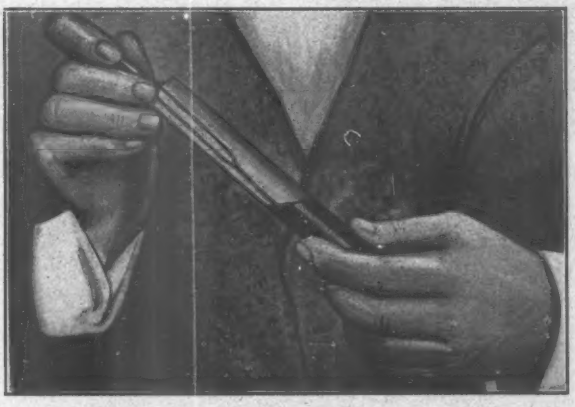

FIG. 3.—Method of introducing media into one of the pipettes.

alcoholic solutions is precipitated by agar-agar, but if some of the indicator solution is titrated with $\frac{n}{10}$ NaOH it is possible to obtain a transparent strongly colored alkaline solution, which can be fixed with the agar-agar medium at a low temperature and produces a brilliant crimson medium. Diamidoazobenzol is not susceptible to such preparation, inasmuch as it precipitates in the form of a bright yellow powder, which is apparently far less sensitive. Litmus, on the whole, is not soluble enough to yield sufficient color for this purpose, and the same may be said of alizarin. We have therefore in Congo red and phenolphthalein two indicators which are capable of demonstrating free acidity, and in the absence of the former, combined acidity. These media are prepared in tubes available at a moment's notice.

Various methods were tried: cubes of agar-agar, beads covered

with the jelly, strips saturated with the same combination, but it was finally decided that capillary tubes gave by far the best results.

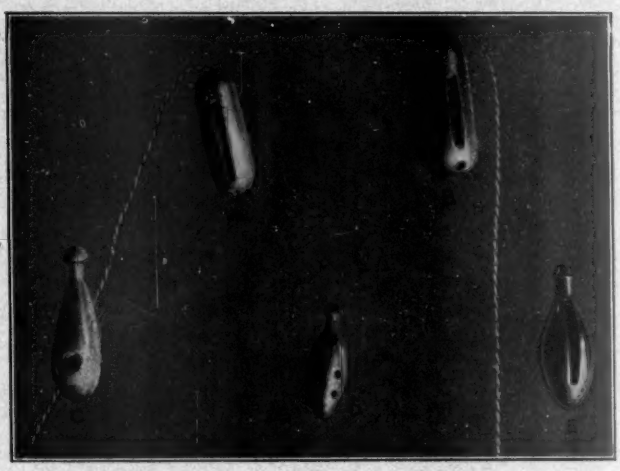

FIG. 4.—*A*, small capsule; *B*, large capsule; *C*, first tip constructed; *D*, Einhorn tip; *E*, modified tip.

These were prepared by drawing out ordinary glass tubing in the usual manner until the diameter approached 1.5 mm. These pipettes were then kept ready for use, and when it was desired to perform a test they were simply plunged into the jelly, withdrawn,

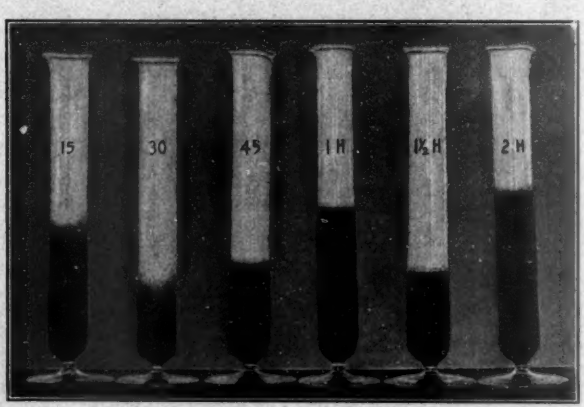

FIG. 5.—Fractional specimens obtained with tip.

and a core of the substance remained in the tube. Pieces were then cut off 8 mm. in length and inserted in the capsule. The capsule

was then given at any stage after a test meal or, for that matter, after an ordinary meal, swallowed in the usual manner, with a little water, and allowed to remain in the stomach ten to fifteen minutes and then withdrawn, taking the precaution to gell the patient to swallow when the capsule reaches the root of the tongue. I usually perform Mett's test *in vivo* by taking one of the capillary tubes, sucking up some fresh egg albumen, holding the pipette over a boiling-water bath for two minutes, which results in a softly coagulated albumen capable of showing peptic digestion. I have been able to demonstrate the digestion of more than 1 millimeter from either end in the course of an ordinary Ewald meal.

While experimenting in Paris with the Einhorn duodenal tube, I became convinced that if the tip was modified, it would be possible to obtain acceptable specimens of the gastric juice. Unfortunately, the tip was so constructed that the perforations, being very minute, became occluded with mucus or alimentary debris, resulting in a small foamy specimen insufficient for testing purposes. Palefski, recognizing the difficulties encountered in this tube, modified it so that the tip instead of weighing 48 grains as does the Einhorn instrument, weighed 105 grains. The great advantage, besides the fact that it could be more easily swallowed, was that it insured a more rapid passage into the duodenum. He used a gold-plated lead ball weighing 105 grains. The following is the table he gives regarding the relative merits of the three tips to which is appended the tip I am about to describe:

Substance:	Gross' perforated, calibrated, lead ball covered with tubing.	Einhorn's perforated brass capsule.	Palefski's perforated gold-plated lead ball.	Author's slotted steel or bronze silver-plated bulb.
Weight, grains	100	48	105	90 to 120
Long axis, inches	½	½	½	½
Size tubing	20 French.	8 French.	8 French.	8 French.
Swallowing	Difficult.	With water.	Easily.	Easily.
Reaches pylorus	Few minutes. By gravity.	Indefinitely.		
Reaches duodenum	..	many hours?	1 to 2 hours	1 to 2 hours

The great advantage of the new tip is the fact that it is slotted instead of perforated, and the slots are so cut that *their diameter is as great as the caliber of the rubber tubing*, in that way assuring the more perfect aspiration of material. It is made of steel, or can be made of manganese bronze; is bulbous in shape, so as to be easily swallowed; weighs from 90 to 120 grains, depending on the extent of the slotting, and when linked with the customary No. 8 French tubing will not only serve as a most acceptable duodenal tube, but finds an even greater field in the study of the gastric contents, capable of being left in the stomach for long intervals, and enabling us to make a fractional study of the gastric juice over the whole period of digestion. The weight is sufficient to permit rapid swallow-

ing, at the same time assisting by gravity its passage through the duodenum. In fact, in making a gastric study, it is repeatedly necessary to caution the patient not to let the tube slip in beyond a certain point, owing to the tendency of the stomach to propel it toward the duodenum. I cannot say that the ordinary Einhorn tip requires as much time to enter the duodenum as the above table would indicate, but I know that there is no comparison between that tip and this one. It is possible in practically every case where no obstruction or lack of motor tone occurs, to enter the duodenum in less than two hours. In our gastric studies this factor must be controlled by regulating the amount of tubing swallowed. A further advantage of this tip is the fact that mucus and food debris as well as juice is extracted, and in this way it is possible to obtain a composite sample of the gastric contents, more than sufficient for testing purposes. I have on repeated occasions obtained twelve graded samples representing the entire cycle of gastric digestion in which some of the samples were 25 c.c. in amount, and none insufficient for quantitative testing purposes. This therefore represents a practical method of following the whole cycle of gastric digestion with a minimum of discomfort, *enabling us to construct a curve which graphically represents every phase.* It is likewise possible to perform lavage and inflation, and recently, on the principle of the stomach whistle, I have attempted to outline the stomach by ausculting the whistling sound which is heard when air is pumped through the tip. Furthermore, about a year ago I was enabled to obtain photographs on one case of the isolated duodenum by the injection of bismuth through the duodenal tube.

The advantages of the capsule are:

1. It offers us a method of inserting practically any substance whether indicators or substances to be digested into the stomach and to withdraw the same when desired.

2. This capsule can be swallowed at any stage in digestion and the condition of the gastric juice read off.

3. In no case have I seen any divergence from the results obtained by the titration of an ordinary Ewald meal, and in one case where both Ewald meal and capsule showed no free hydrochloric acid, the capsule on the same patient with a mixed diet showed a trace of this substance which was confirmed by subsequent examination.

4. Various substances, like meat, can be inserted into the capsule and gastric digestion observed.

5. It should be of value in determining the presence of an acid rest in the stomach. Its weight assisted by the swallowing of a little water will rapidly propel it to the bottom of the stomach and the possibility of gastrosuccorrhea may be demonstrated.

6. The preparation of the indicator media is easy and requires no sterilization.

7. The size of the capsule is such that it can be swallowed by anyone with practically no discomfort, and even in infectious condition the condition of digestion can be recorded.

8. Although esophageal and pharyngeal secretions can penetrate the slots of the capsule, they can in no way vitiate the result, as they can act only on the extreme end of the capillary tubes, while in practically every instance the reaction takes up one-half of the tube or more.

It is hoped that further methods can be elaborated for the use of this capsule in the future.

Briefly the advantages of the modified tip and tube are:

1. It represents a practical method of fractional testing of gastric secretion, observing the entire cycle of gastric digestion, and following the transit through the duodenum.

2. By this method inflation and lavage can be performed and the organ delimited by auscultation as outlined above.

3. The great advantage of the present tip besides the fact that it embodies the weight and the form best suited for the purpose, is that its slotting is of such size and form as to represent the maximum caliber of the tubing and permit us to obtain a composite sample of the juice.

OSTEITIS DEFORMANS (PAGET) INVOLVING A SINGLE BONE: REPORT OF A CASE.

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Osteitis deformans (Paget) belongs to the rare affections of bone. Within recent years more interest has been taken in this malady, as is evidenced by the appearance in the literature of numerous case reports, some containing valuable additions to our knowledge of the pathogenesis of this disease.[1] Among the cases of osteitis deformans described in the literature there are instances in which the disease remained limited to one or two bones.[2] Some of these descriptions are accompanied by histological and radiographic studies, which make it fairly certain that they are genuine examples of Paget's disease, since the pathological changes observed in them correspond with those pictured by Paget[3] and Butlin.

[1] Recently I had the opportunity to study six typical cases of Paget's disease admitted to the Johns Hopkins Hospital and Dispensary. Hurwitz, Johns Hopkins Hosp. Bull., September, 1913.

[2] The existence of such localised forms of hyperostosis has led some authors to regard leontiasis ossea (hyperostosis cranii) not as a separate disease entity, but as a form of osteitis deformans in which the morbid process is confined to the bones of the cranium. Prince, Trans. Assoc. Amer. Phys., 1902, xvii, 386.

[3] Med. Chir. Trans., 1877, lx, 37.

The following case record is of clinical interest, since radiographic study shows that in this patient the disease was limited to one bone, the right femur, although the malady lasted for about four or more years.

CASE (Disp. No. F. 9283).—J. M., white, aged fifty-six years. In July, 1913, the patient came to the Johns Hopkins Hospital dispensary complaining of pain in "both hips and in the small of the back."

Family History. There was no history of any unhealthy inheritance; the patient's father died of "Bright's disease" at the age of fifty-nine years; his mother died during childbirth. All of the members of his father's and his mother's family were well. The patient was not aware of the existence of tuberculosis, heart disease, cancer, rheumatism, nor gout in any members of his family; none of them had suffered from a similar malady. The patient has been married for twenty-five years; he had had two children, one son and one daughter; both of his children were well. His wife had one miscarriage twelve years before.

Personal History. The patient could not recall any diseases of childhood. He had always been a robust young man. At the age of eighteen years he had typhoid fever and "meningitis"(?); this illness lasted about three or four months and terminated uneventfully. When twenty-two years old he had a venereal sore, which lasted a few weeks and yielded to treatment; the exact nature of this lesion was not clear; there was no history of any secondary luetic manifestations. Five years later he had a gonorrheal infection. Fifteen or eighteen years before the patient was accidentally shot in the right leg; two bullets penetrated his body, one passing through the soft parts of the middle third of the right thigh and the other a little above this point. According to the statement of the patient's physician at that time the bullet did not penetrate the bone. After a few weeks' illness the patient recovered completely and no impairment of function of the limb followed this accident.

Present Illness. For thirty-five years the patient suffered from intermittent pain in the back. Except for this pain he considered himself well up to four years before, when he was fifty-two years old. At this time he began to complain of "rheumatism" in the hip-joints and in both legs. The pain was not entirely confined to his joints, at times he experienced a cramp-like pain in the calf muscles, which would "draw up into a knot." Shortly after the onset of these symptoms the patient's friends noted that he was limping. The patient himself had not been aware of this. One year before he consulted a physician, who told him that his right leg was bowed and that it was about three-quarters of an inch shorter than the left. To equalize this difference in the lengths of the two extremities the patient began to wear a higher heel on the right shoe. The patient considered the pain in the back worse than that in the legs;

it was of a dull, intermittent character, entirely absent during sleep, and in the waking hours it was worse when the patient stood than when he walked. His average height had been 5 ft. 10½ inches; his weight had varied between 170 and 180 pounds. He did not believe that his head had changed in size, for he had always worn a No. 7¼ hat with comfort.

Physical Examination. July 10, 1913. The patient was a well-nourished man of large frame and good stature; height, 5 feet 6 inches. There was well-marked alopecia capitis and pigmentation of the exposed parts; the mucous membranes were of excellent color. The patient looked unusually robust and normal in appearance.

Skeletal System. There was nothing, on general inspection, which would attract the observer's attention to the bony framework. The patient stood slightly inclined toward the right, which appeared to be due to the outward and anterior bowing of the right thigh; this explained also the downward tilting of the pelvis on the right side, and accounted for the limping gait.

The head appeared massive, but not out of proportion to the rest of the bony framework; the calvarium was prominent, but it was not enlarged in comparison with the features.

MEASUREMENTS OF THE HEAD.

	Cm.
Occipitofrontal circumference (maximum)	57.0
Occipitofrontal diameter	19.5
Occipitomental diameter	21.5
Biparietal diameter	15.5
Suboccipitobregmatic diameter	17.0
Suboccipitobregmatic circumference	54.5
Bitemporal diameter	15.0
Circumference of vault from meatus to meatus	38.0

Thorax. The thorax presented no special abnormalities; it was somewhat barrel-shaped; its circumference at the top of the axilla measured 95 cm.

Spine. There was no evidence of kyphosis or scoliosis at any level of the spine. On pressure over the spine in the cervical and dorsal regions no tenderness was elicited; in the lumbar region, however, the erector spinæ group of muscles were held spastic, obliterating the normal lumbar lordosis; pressure over this region caused pain. There was no pain directly over the sacro-iliac articulations. The range of motion of the spine was fairly good in all directions.

The bony pelvis was not broader or heavier than normal; the distance between the lower border of the ribs and the iliac crests was not decreased. Measurements of the pelvis showed the following: intercristal diameter, 29 cm.; interspinous diameter, 25 cm.; intertrochanteric diameter, 32.5 cm.

Upper Extremities. The arms did not appear disproportionately long. Both humeri were straight; no thickening or roughening could be made out on palpation. The radius and ulna on both sides were straight and showed no abnormalities. The grand expansion of the arms measured 171.25 cm. (68.5 inches).

Lower Extremities. The right lower extremity presented the special point of interest; the right thigh was markedly bowed anteriorly and laterally; the bowing was considerable, so that with the heels together the internal condyles of the femora were separated a distance of 4.5 cm. On palpation the right femur was found to be more massive, thicker, somewhat more nodular, and rougher through its whole length than its fellow. There was no tenderness elicited on deep pressure, and there was no evidence of any local inflammatory lesion. On extending the leg and flexing the thigh upon the abdomen, more pain was caused on the left side than on the right, due to a relaxation of the hamstring muscles beneath the bowed right femur.

MEASUREMENTS OF THE LOWER EXTREMITIES.

	Cm. right.	Cm. left.
Anterior superior spine to internal malleolus	86.0	88.5
Umbilicus to internal malleolus	98.5	100.0
Anterior superior spine to internal condyle of femur	47.0	49.5
Circumference of thigh 20 cm. above midpatellar region	47.5	46.0
Circumference of calf 20 cm. below midpatellar region	30.5	30.5
Circumference of ankles above malleoli	19.5	19.5

From the measurements it was evident that the right leg was 2.5 cm. shorter than the left, and that the shortening of the whole leg, as measured from the anterior superior spine to the internal malleolus, equaled the shortening of the right femur as measured from the anterior superior spine to the internal condyle; therefore, the shortening of the right leg was due entirely to shortening of the right femur.

Both tibiæ appeared straight; there was not the slightest anterior or lateral bowing. On palpation both bones felt normal.

General Examination. The temporal arteries were not tortuous. Eyes were not prominent; pupils reacted to light and on accommodation; extra-ocular movements were good. Teeth were slightly carious; there was extensive dental work. Pharynx was negative. There was no general glandular enlargement.

Lungs. Hyperresonant; clear on percussion and auscultation.

Heart. Cardiac dulness extended 12 cm. to the left and 4.5 cm. to the right of the midsternal line; heart sounds were clear. Pulse showed no abnormalities; blood-pressure, 140 (Tycos).

Abdomen. Normal to inspection. Liver dulness extended to the costal margin. Spleen was not palpable.

Reflexes. Present in both upper and lower extremities.

Wassermann reaction was negative in May, 1913.

Radiographic Examination (skiagram Nos. 18334 and 18965. Reported by Dr. F. H. Baetjer). *Skull:* Skull showed slight diffuse chronic thickening of inner and outer tables. Exostosis at occipital tuberosity. Sella normal in size and shape; solid sella. Calcification of pineal body. *Right femur* (Fig. 1): Femur showed well-marked bowing. Head of femur was bent, producing coxa vara. There was chronic diffuse thickening of entire shaft of femur; medullary canal could be easily made out and did not seem to be involved. Thickening through shaft of bone was uniform throughout, with some slight interlinear striations. Notwithstanding the fact that there were pieces of bullet scattered throughout the leg, the condition did not impress one as an osteomyelitis, but rather as Paget's disease. *Left femur:* Normal in every respect. *Right tibia and fibula:* Slight periostitis of tibia; fibula showed normal variation.

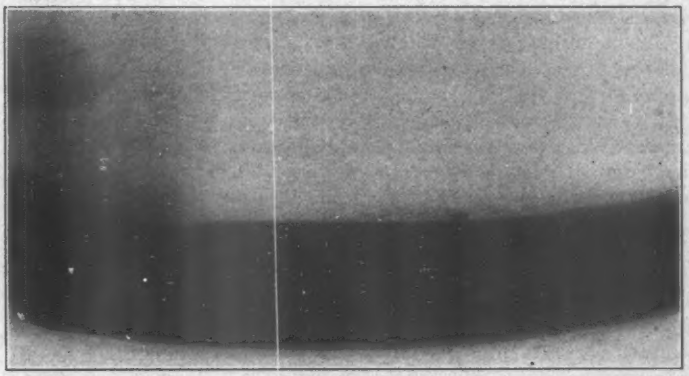

FIG. 1.—Skiagram of right femur, showing bowing and chronic diffuse thickening of entire shaft of the bone. (Thickening of shaft of bone is uniform throughout, with some slight interlinear striations). Medullary canal can be easily made out and does not seem to be involved.

Summary. There were certain points in the history and examination of this patient which deserve special mention: (1) the history of typhoid fever at the age of eighteen years, the possible history of lues, with the slight periostitis of the right tibia (Wassermann reaction negative), and the history of a gunshot wound in the right thigh fifteen or eighteen years before, must be kept in mind as a possible etiology for the deformity, although the subsequent history and radiographic study did not support this view; (2) the insidious onset, at the age of fifty-two years, of bowing and thickening of the right femur, and the characteristic association of this deformity with vague rheumatic pains; (3) the remarkable localization of the morbid process in one bone, although the disease had

lasted probably for a period of more than four years; (4) the presence in the skiagrams of the right femur, of the bony changes which characterized the disease, and their absence in other bones.

The name ostitis deformans was given by Czerny[4] to a disease of bone described by him in 1873. The subject of this disease was a young soldier, aged twenty-two years, who subsequent to the exposure and fatigue of a military campaign began to suffer from continuous pains in the left leg, followed in several months by the spontaneous development of curvature in the tibia and fibula of this leg. Because of the sequence of the pathological changes observed in these bones—softening, bending, and hardening—Czerny was inclined to regard the condition as a chronic inflammation rather than as a localized form of osteomalacia.

Three years later, Sir James Paget[5] used the term osteitis deformans for a well-defined and slowly progressive disease which now bears his name. Unlike the localized malady described by Czerny, the disease described by Paget is characterized clinically by an involvement of a large part of the skeleton. According to him the affection is usually symmetrical, and attacks most frequently the skull and the long bones of the lower extremities; the latter enlarge, soften, and become unnaturally curved and misshapen. It would appear, therefore, that, although clinically different, the same pathological process underlies the localized as well as the more generalized form of this obscure disease of bone.

Since the appearance of the communications by Czerny and by Paget a considerable number of cases characterized by bending and hardening of one or two long bones have been reported as instances of Paget's disease, although the exact relationship of these two disease types is still not clear. Some authors are of the opinion that "multiplicity of the bones affected is the constant characteristic"[6] of the disease described by Paget. Schirmer,[7] however, concludes from his collective study that there are true instances of osteitis deformans (Paget) in which for years the deformity remains limited to one bone, and in which it is difficult to predict whether or not the disease will progressively involve other parts of the skeleton. This view is also held by Schlesinger,[8] who designates the localized as the "monoösteitic" form of osteitis deformans; whereas both Stegmann[9] and Latzko[10] maintain that the etiology of the morbid process which leads to the bending and thickening of a single bone is, in all probability, different from that of Paget's disease.

CASES OF OSTEITIS DEFORMANS (MONOÖSTEITIC FORM) RECORDED IN THE LITERATURE.—A critical analysis of the cases reported in

[4] Wien. med. Woch., 1873, xxiii, 894.
[5] Loc. cit.
[6] Fitz, Trans. Assoc. Amer. Phys., 1902, xvii, 398 and 402.
[7] Centralbl. f. d. Grenzgeb. d. Med. u. Chir., 1908, xi, 561, 609, 641, 689, 721.
[8] Mitteilungen d. Ges. f. innere Med. u. Kinderheilk., Wien, 1907, vi, 61; ibid., 1908, vii, 99.
[9] Katholicky, Wien. klin. Woch., 1905, xviii, 619 and 649 (Discussion).
[10] Ibid.

the literature as osteitis deformans (Paget) in which the disease remained limited to a single bone shows that a small number only properly belong to this group. Many of the others, as will appear later, are definitely instances of luetic osteitis, bone tumor, sarcoma, carcinoma or myeloma, and of spontaneous fractures, with bending and with thickening due to excessive callus formation.

Studies of the morbid anatomy of osteitis deformans (Paget) have led to the knowledge that this disease is associated with pathological changes in the bone which are, more or less, constant; in the main, the pathological findings of Paget[11] and Butlin have been confirmed by later investigators, von Recklinghausen,[12] Stilling,[13] Packard, Steele and Kirkbride,[14] and Higbee and Ellis.[15] Moreover, studies of skiagrams of bones affected with Paget's disease have made it possible not only to recognize the gross pathological anatomical changes during life, but to differentiate them from other morbid processes affecting one or more long bones, especially those of syphilitic origin.[16] It would be well, therefore, to accept at present as instances of Paget's disease only those cases which have been confirmed either by pathological or radiographic study.

Of this localized form of the affection there are probably not more than five or six cases recorded up to the year 1908, in which pathological or *x*-ray study has confirmed the clinical diagnosis. Bowlby,[17] in 1883, described a case of osteitis deformans in which the right femur alone was involved. This case I should like to present in some detail, since a search of the literature shows that it is the only other instance of proved Paget's disease on record in which one femur alone was involved:

"C. G., aged sixty-four years, a cabman, was admitted to St. Bartholomew's Hospital on August 23, 1882, suffering from an injury to the head, which caused death fourteen days later. No measurements of the thighs were made during life, and the patient was not in a condition to give any history of his previous health; it was noticed, however, that the right femur was much curved in an outward and forward direction, and was shorter than its fellow. After death his son, who was an intelligent man, told me that his father's leg had gradually become curved during the last ten years of his life, that it had not caused him any pain, and that he had frequently measured both limbs, with the view of ascertaining the amount and progress of the shortening, which a few months before death amounted to two and a half inches. He had often suffered from gout, mostly in the great toe, but was otherwise healthy. A postmortem examination showed that the only bone affected was the femur of the left (?) side."[18]

[11] Loc. cit.
[12] Virchows Arch., 1890, cxix, 542.
[13] Jour. Med. Research, 1911, xix, 55.
[14] Trans. Path. Soc. Lond., 1883, xxxiv, 192.
[15] Festschr. d. Assistenten f. Virchow, 1891.
[16] Trans. Assoc. Amer. Phys., 1901, xvi, 666.
[17] Zeitschr. f. Heilk, 1902, xxiii, 130.
[18] Ibid, 193.

The most striking features made out from a pathological study of this diseased bone are noted in the description of the photograph of the specimen reproduced from the *Illustrated Medical News* for February 23, 1889, which contains an abstract of this case (Fig. 2).

FIG. 2.—Osteitis deformans involving a single bone. (After Bowlby, illustrated Medical News, 1889, ii, 188). Shows curvature of femur; shaft is increased in circumference. Neck of bone is placed at right angles to shaft. Medullary canal is irregular in shape; its caliber is encroached upon by new bone, partly of a hard porcellaneous appearance and partly of a cancellous nature.

A similar case, reported by Benno Schmidt[19] about ten years earlier, has additional interest, since during the period of observation, four years, the disease subsided in the right femur, where it began, and involved the left tibia. The patient was an apothecary, aged fifty-six years; he gave no history of trauma, lues, or other infections. According to the patient's account he began to have pain in the right thigh, and later noticed that his right femur was beginning to bow. The right leg became 2 cm. shorter than its fellow. About four years after the onset of the malady the process subsided in the right femur only to begin in the left tibia. Unfortunately the diagnosis of this case was not verified by anatomical study. The record is of interest because it shows that this disease may remain localized in one bone for a number of years, only later to manifest itself in some other part of the skeleton, and that patients who are reported to have this affection in one bone may develop it later in its more generalized form.

More recently Schmieden[20] and Katholicky[21] have reported a single case, and Schlesinger two cases of this "monoösteitic" form of osteitis deformans. In every one of these cases a characteristic feature was involvement of one tibia. The diagnosis was confirmed in each instance by histological or radiographic study.

Schmieden's patient was a woman, aged fifty-eight years, without a history or stigma of lues. At the age of fifty-two years, without

[19] Arch. f. Heilk., 1874, xv, 81
[20] Deut. Zeitschr. f. Chir., 1903, lxx, 207.
[21] Loc. cit.

apparent cause, she gradually developed thickening and bowing of the right tibia. No similar changes were demonstrable in any other bones of the body. Histological examination of material obtained, first by an osteotomy and later by amputation, showed the pathological features to which reference already has been made: disappearance of the normal bone, its replacement by osteoid tissue, with a destruction of the fatty marrow, and its conversion into connective tissue. In this particular case, skiagrams showed that the cortex had almost disappeared, and it was apparent from microscopic study that the process of bone absorption had progressed more rapidly than that of new bone formation.

Similarly, Katholicky's patient also was a woman, aged sixty years, who for ten years had observed that her tibia was gradually bending and thickening; the fibula remained normal and straight, and looked like a string to a bow represented by the bent tibia. It was demonstrated by *x*-ray examination that the entire lamellar architecture of the tibia was changed, and that there was evidence of decalcification and new bone formation.

Both of Schlesinger's[22] patients were men, one aged sixty-two years, and the other sixty-four years; in both the right tibia was the only bone affected. The first patient was observed twelve years, and during this interval no other bone became diseased, not even the fibula of the same extremity. In both cases the typical changes of Paget's disease were present on *x*-ray examination.

Schlesinger is inclined to place all such instances of osteitis deformans, with involvement of a single bone, into a special group which he calls the "monoösteitic" form of Paget's disease. This form he characterizes as follows: "The disease begins insidiously without trauma (without a history of lues), may continue for years without attracting the patient's attention, and is usually discovered accidentally. In all of the author's three cases the changes were well advanced before the disease was discovered by the physician. Pain appears to be absent; in this respect it differs from the types described by Joncheray, of which the painless form affects only the upper extremities. The power of walking is not greatly interfered with, even though the deformity of the tibia (thickening and bending) is far advanced. This point has been emphasized by Paget also. The disease affects the tibia, and as it appears, especially in front. It does not progress in spite of years' duration and apparently involves no other bones."[23]

Besides the cases mentioned, there are on record a number of examples which may belong to the "monoösteitic" form of Paget's disease. In most of these the clinical diagnosis has not been substantiated by anatomical or *x*-ray examination, and the clinical facts presented are so meager as to make one question whether

[22] Loc. cit. [23] Mitteilungen d. Ges. f. innere Med. u. Kinderheilk, Wien, 1908, vii, 101.

they are really instances of this disease at all. To this doubtful group belong the cases which Czerny[24] collected from the literature: those of Scoutetten, Solly, Mosetig, and Weinlechner. The clinical descriptions of their patients are not convincing; besides all of them, with one exception, the second case of Solly, were not over thirty years of age at the time the disease began; whereas it is rare for osteitis deformans to begin before the fifth or sixth decades. Likewise the patient of Volkmann[25] was a boy, aged nineteen years, in whom the left tibia became bent spontaneously; Volkmann regarded this as an instance of chronic osteitis, but its identity with osteitis deformans (Paget) is doubtful.

In their dissertations on osteitis deformans both Patschu[26] and Glinèr[27] cite a number of examples in which the disease affected one bone. In each instance the diagnosis was based upon unverified clinical observation; from these it is obvious that a large number of the cases mentioned belong to diseases other than osteitis deformans. The case of Isreal, for instance, which both authors classify under osteitis deformans, proved after amputation to be a fracture of the left femur, with dislocation of the fragments and excessive callus formation; again, the patients of Martini and of Küster were both suffering from pathological fractures of the femur at the site of tumors. So, too, the case of Wolff, cited at some length by Patschu, is another instance of pathological fracture rather than of osteitis deformans. It is evident, therefore, that numerous unrelated affections have been improperly classified as osteitis deformans.

Differential Diagnosis.—The generalized form of osteitis deformans (Paget) presents so characteristic a clinical picture that it is easily recognized; but the more localized form of the disease, especially when the affection remains limited to one bone for many years, presents difficulties for diagnosis because it may resemble very closely other affections of bone. Syphilitic disease of bone, osteitis fibrosa, and certain other diffuse new formations of bone may resemble the "monoösteitic" form of osteitis deformans.

Syphilitic disease of bone, like syphilitic disease of other tissues, may imitate other affections of bone so closely that it must always be borne in mind in any bone disease where the diagnosis is in doubt. Syphilitic periostitis with bone formation is a frequent lesion, especially in congenital lues. In this condition the tibia is most commonly involved; the bone is usually curved and shows a rarefying and condensing osteitis, with irregular periosteal and endosteal new bone formation. The condition may simulate so closely osteitis deformans that it has been designated osteitis deformans syphilitica.

[24] Loc. cit. [25] Beitr. z. Chir., 1875, p. 148.
[26] Ueber deformierende ostitis, Dissertation, Berlin, 1880.
[27] Ueber ostitis deformans (Paget), Dissertation, Bern., 1910.

Few general rules are of value in so protean a disease as syphilis, but some of the following points may be of help to differentiate clinically the two conditions: (1) In acquired syphilis the bones of the cranium are more frequently involved than the long bones; in congenital syphilis, where the long bones, especially the tibiæ, are most frequently the seat of the disease, the patients are young, whereas osteitis deformans (Paget) usually affects patients late in life; (2) in the syphilitic cases, in addition to the general enlargement, the affected bones often present irregular bosses on their surface; (3) in syphilitic disease, lesions, either of other bones or the soft tissues, are likely to be present at the same time; in congenital syphilis other obvious signs of the disease may exist; (4) the presence of osteoscopic pains is an important feature of syphilitic disease of bone; the pain is worse at night, is usually continuous, and has a boring character. In osteitis deformans the pain presents no constant characteristics; (5) in most cases of syphilis of bone the effect of treatment is usually pronounced; improvement under treatment to be of diagnostic value, however, must be marked and sustained; (6) careful study of the skiagrams of syphilitic bone affections and of osteitis deformans has shown that the two diseases can be differentiated radiographically.

Ostitis fibrosa (v. Recklinghausen's disease of bone; tumorbildenden ostitis deformans) is essentially an osteomalacia deformans which may involve the entire skeleton or appear in isolated portions; in the latter location it may be mistaken for osteitis deformans of the type under consideration.

Pathologically ostitis fibrosa and osteitis deformans are closely related, and some authors contend that the two diseases cannot be differentiated histologically. V. Recklinghausen, however, considers the disease described by him a separate entity, and emphasizes certain points of difference: in ostitis fibrosa there are regressive changes of the fibrous marrow into gelatinous cysts, and progressive changes leading to the formation in the long bones of small, brown, red tumors of the nature of giant-celled sarcomas; in osteitis deformans the bones are usually more curved and histological, and *x*-ray studies show that in this disease the changes in the bone marrow are less marked and the process of new bone formation more striking than in the type described by v. Recklinghausen. The two affections are unlike in another important respect, which is useful in the differentiation of these two conditions clinically: the occurrence of spontaneous fractures is almost pathognomonic of ostitis fibrosa, and according to Brunn,[28] it is one of the earliest indications of the existence of this malady; in osteitis deformans, on the contrary, spontaneous fractures are rare. Among 86 cases collected from the literature by Schirmer[29]

[28] Beitr. z. klin. Chir., i, 72.

[29] Loc. cit., p. 646.

in 1908 there were only five instances of osteitis deformans associated with spontaneous fractures.

Of other forms of diffuse hyperostosis which may be limited to one bone and produce a clinical picture like localized osteitis deformans, two only deserve brief mention. One form is seen around osteomyelitic cavities, where, owing to a diffuse thickening of the spongy bone in association with a necrosis of the marrow cavities, hard new bone is formed; the process may involve also the compact bone and lead to considerable thickening of the shaft of the bone over a greater or less area. This condition can usually be differentiated from osteitis deformans by the history and the clinical symptoms given by the patient and by *x*-ray examination.

Another form of diffuse hyperostosis results from the complete ossification of an exuberant callus such as sometimes occurs after a fracture. Where this process is limited to a single bone it is readily differentiated from the "monoösteitic" form of osteitis deformans by the history and *x*-ray examination.

Although Paget's disease has been called by Katholicky and by Schmieden osteomalacia chronica deformans hypertrophica, clinically this affection and osteomalacia or halisteresis have little resemblance. Pathologically they may have this in common: in both diseases decalcification and softening of bone occur; in osteomalacia the process stops at this point, whereas in osteitis deformans decalcification is associated with new bone formation.

VALVULAR HEART DISEASE CONSIDERED AS A CONTRIBUTORY ETIOLOGICAL FACTOR IN PULMONARY TUBERCULOSIS: A COMPLICATION OF THE FIRST MAGNITUDE.

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In the clinic at North Reading I have taken particular interest in deriving a careful history relating to general and occupational habits of such cases of pulmonary tuberculosis as have exhibited definite signs of valvular heart disease. For from the matter of these histories it has appeared oftentimes quite suggestive that the cardiac disease has handicapped the patient's resistance to such an extent as to permit implantation and progress of tubercular disease.

In addition, I have kept clearly in mind the identity of each patient affected with this important complication, in order that I might modify or supplement in these cases the instructions laid down

for the care and treatment of tubercular patients. The resulting success in handling the patients in this manner and in directing their after-care has demonstrated at least to my mind a superiority of method which would not be obtained by regarding the cardiac irregularity only in a minor light.

In the first place, the supposition that valvular heart disease may predispose an individual to pulmonary tuberculosis is the antithesis of the accepted view established in the early part of the last century, and more or less adhered to down to the present time.

In 1844 Rokitansky's[1] almost classic assertion was made that those diseases of the heart and bloodvessels producing cyanosis were not compatible with tuberculosis, the cyanosis causing an "exquisite immunity." Again, the same author[2] made the statement convincingly that there was "the greatest practical importance in the fact that mechanical obstacles in the centre of the circulating system, or rather the heart producing increased 'venosity' in the lungs with resulting cyanosis, proceeded to act against tubercle." Pottenger[3] believed Rokitansky's observations on the coincidence of heart disease and tuberculosis have been generally confirmed by modern observers, and explained the relative infrequency of dual occurrence to the fact that the hyperemia taking place in the lung in some forms of heart disease, caused therein a concentration of the blood with its protective bodies. The Bier method[4] of treatment of tubercular parts by hyperemia was established through discovery that stenosis of the pulmonary artery, inducing anemia of the lung, was followed by pulmonary tuberculosis in a large percentage of cases, and, conversely, that hyperemia apparently had an immunizing power against tuberculosis of the lungs.

R. C. Cabot[5] states that about one-quarter to one-third of all cases of pulmonary stenosis are complicated with pulmonary tuberculosis. However, he makes no mention of any antagonism of other forms of morbus cordis against pulmonary tuberculosis, nor does he venture an opinion as to the real factor in the causation of pulmonary tuberculosis in pulmonary stenosis cases, whether it may be anemia of the lung or the subnormal resistance of cardiac cases in general and pulmonary stenosis cases in particular. In this last respect, Babcock[6] mentions that the congenital forms of pulmonary stenosis render the individuals weakly, undersized, and sometimes mentally deficient, and that they manifest a striking cyanosis. Therefore, we should expect them to be quite promising subjects for the growth and progress of tuberculosis.

Lawrason Brown[7] speaks of the deviation of opinion upon this

[1] Handbuch der path. Anat., 1844, Band II, S. 520.
[2] Ibid., 1846, Band I, S. 427.
[3] Pulmonary Tuberculosis, 1908, p. 211.
[4] Pottenger, loc. cit.
[5] Physical Diagnosis, 4th ed. p. 252.
[6] Diseases of the Heart and Arterial System, p. 380.
[7] Amer. Jour. Med. Sci., 1909, cxxxvii, p. 186.

subject, and quotes Vierordt, who maintained that whatever frequency of occurrence there was of pulmonary tuberculosis in pulmonary stenosis cases was due to the lack of vitality and resistance common to any individual suffering from any congenital heart disease. Johanne Otto[8] has stated that the simultaneous occurrence of the two lesions, that is, cardiac and pulmonary, is by no means incompatible, and, as a matter of fact, is rather ordinary in women especially, on account of lowered vitality due to the heart disease. She further averred that malnutrition of the cardiac muscle and insufficient compensatory hypertrophy, seen often in women, are conditions which render a tubercular infection more readily possible.

Hermann Vierordt[9] took exception to Rokitansky's views, particularly concerning pulmonary stenosis as a cardiac lesion, and said that patients suffering from this variety of organic heart disease were predisposed to pulmonary tuberculosis.

Norris[10] quite completely covers the ground relating to the concurrence of heart disease and pulmonary tuberculosis in an excellent dissertation in which he supported Vierordt's belief that the frequent occurrence of pulmonary tuberculosis was not limited to pulmonary stenosis alone, but is noted also in other varieties of congenital heart disease. He, however, did not believe pulmonary tuberculosis any more frequent in pulmonary stenosis or atresia than in the case of other conditions in which nutrition is profoundly impaired. Babcock believes that anything which like valvular disease impairs nutrition must necessarily lessen the likelihood of successful resistance to tuberculosis, and that when the combination of the two does occur it enhances the gravity of the prognosis, for they cannot fail to react injuriously on each other.

Osler[11] speaks of "a temporary disturbance of compensation" as a possible occurrence in heart disease when the loss of reserve force exists for a short and limited time and does not go on to complete decompensation. This interval seems attractive when considering the opportunity for implantation of pulmonary tuberculosis in an individual, for we might reasonably expect that at just such time when he is overcome by fatigue that he is all the more susceptible to infection. Since, as Osler says, reserve power of the normal heart can be affected abnormally by any interference with the cardiac muscle, such as infection, intoxication, and malnutrition, there must be a considerably larger adverse effect in the case of a morbid heart with its lessened reserve capacity and greater irritability. Poorly nourished, as many pretubercular individuals are, and with less strength to spare, it seems rightly conceiv-

[8] Das Ausschliessungs verhältniss zwischen Herzklappenfehlern und Lungenshwindsucht, Virchows Archiv, 1896. Bd. cxliv.

[9] Specielle Pathologie und Therapie, H. Nothnagel, XV. Band, II. "Die angeborenen Herzkrankheiten," p. 97. (Pulmonalstenose und Tuberculose.)

[10] Tuberculosis and Heart Disease, AMER. JOUR. MED. SCI., October, 1904, p. 655.

[11] Modern Medicine, vol. iv, p. 210.

able that certain cardiac patients should be oppressed with the united conditions of subnormal resistance and overfatigue, the latter an invitation to infection and the former a frank admission of insufficient protection. Therefore, Sir William Collins' quotation has its significance: "The germ has, perhaps, been too much with us, and the paramount importance of soil has been absurdly underrated."[12]

There seems to be considerable variation among the published statistics concerning the incidence of pulmonary tuberculosis and valvular heart disease. At one extreme we have Kryger's[13] figures in 1100 autopsies on tubercular subjects, in which only 10, or 0.9 per cent., showed cardiac disease, while in 59 autopsies on valvular disease cases all had healed or arrested tuberculosis.

Norris[14] collected figures from the literature covering 8154 autopsies on tubercular subjects where 3.5 per cent. showed signs of valvular heart disease. He relates that the coincidence of valvular disease and pulmonary tuberculosis is encountered with only moderate infrequency, but that this condition has been more often recorded by recent than by old observers. He further reported 130 cases (7.3 per cent.) of valvular disease in 1764 autopsies which he himself performed on tubercular subjects.

Anders[15] noted a 1.2 per cent. incidence in 10,687 cases at autopsy. L. Brown[16] noted a figure as low as 0.9 per cent. valvular heart disease in a grand total of 71,115 cases of records collected abroad.

Carrington[17] has reported 21 per cent. heart disease cases occurring in another series of cases of tuberculosis.

An autopsy report of the Phipps Institute[18] noted organic disease of the heart and lungs as occurring coincidentally in 10.3 per cent. of 143 cases. Mitral were found to preponderate over aortic lesions. Comment was made upon the frequency with which the two conditions occurred together and the conclusion drawn that the tendency of clinical records is rather to underestimate than to overestimate this frequency.

In a later report[19] from the same institution five cases of incompetency of the heart valves were found (6.7 per cent. in the 74 autopsies performed that year. The mitral valve was affected four times and the aortic twice. A summary for three years stated 21 valvular incompetencies or 0.6 per cent. in the 197 cases autopsied.

Shultze[20] found antecedent cardiac disease 42 times in 109 cases

[12] Draper's Research Memoirs. Karl Pearson, Studies in National Deterioration, II.

[13] Ueber das gleichseitige Vorknommen von Lungentuberculose und Klappenfehler des linken Herzens, Münchener Dissertation.

[14] Loc. cit.

[15] Amer. Jour. Med. Sci., 1909, cxxiii, p. 93.

[16] Brown loc. cit.

[17] Cited by Norris, loc. cit.

[18] Phipps Institute, Second Anual Report, 1904–1905.

[19] Phipps Institute, Fifth Annual Report.

[20] Cited by Norris, loc. cit.

of tuberculosis, while similar instances might be quoted almost indefinitely.

L. Brown[21] believed that the difficulty in reconciling the great differences among these figures was explained by the indifference with which tuberculosis has been treated at many general hospitals and the reluctance of some pathologists for performing autopsies in apparently uncomplicated cases of tuberculosis. Therefore, he thought the occurrence of the larger percentages of heart disease found by some pathologists might be readily explained. In my own experience many instances have come to light of patients admitted to the North Reading State Sanatorium with frank and long-standing heart disease complicated with pulmonary tuberculosis; and yet their application commitment papers made out and signed by their physician recorded no mention of their heart disease, the heart repeatedly being noted as "negative." In 46 cases where this complication existed the writer found only 6 wherein any mention of heart disease was made by the committing physician. These papers were selected at random from the 1400 application forms filed in our central office. Eighteen "negative," "heart normal," or "O.K." notations were found in the spaces reserved for heart examination records although they related to patients with frank valvular heart disease.

Accordingly, we are not always impressed by gross statistics regarding the coincidence of valvular heart disease and pulmonary tuberculosis, and we are less reluctant to state the results of our investigation at North Reading, although these, as compared with some of the low figures found in the literature, would appear rather startling.

In reviewing 1300 consecutive case records of patients admitted to and treated at the North Reading State Sanatorium in the past three years, my interest was aroused in this particular subject by the rather frequent occurrence of record of heart murmurs detected by the various members of the medical staff. To be sure, not all such adventitious sounds indicated organic disease of the heart, as many were attributed "functional," "cardiorespiratory," or "undetermined."

However, without further mention of the undetermined murmurs, we found definite records of valvular heart disease in 228, or 17.53 per cent. of the 1300 case reports examined. Of the 605 female cases, 128, or 21.15 per cent. had cardiac disease, and of the 695 male cases, 100, or 14.3 per cent. were similarly complicated; of the former 74, or 57.8 per cent. were diagnosed as mitral regurgitation, 42 or 33.5 per cent. as mitral regurgitation and stenosis, and 12, or 9.3 per cent. as aortic regurgitation, 3 of the latter having also aortic stenosis, and 2 others of the 12 having mitral regurgitation with aortic regurgitation.

[21] Loc. cit.

Of the men, 65 had mitral regurgitation, and of these 65 there were 28 showing also mitral stenosis. Aortic regurgitation appeared in 24 records, and together with aortic stenosis in 6 cases. 5 cases were recorded as "undertermined" in character, although noted as "valvular heart disease." Two of these were suggestive of tricuspid insufficiency according to the record, but no definite diagnosis as such was made.

It should be stated that approximately 75 per cent. of all cases admitted to the North Reading State Sanitorium have been in the third stage at time of admission. Some question, therefore, might be raised as to whetehr the valvular trouble was actually the primary disease. On this point L. Brown[22] believed that very rarely did endocarditis occur in pulmonary tuberculosis, and that still more rarely was it a case where the tubercle bacillus was the infecting organism.

When heart disease of the inflammatory valvular type did develop during the course of pulmonary tuberculosis it was most often a late complication. He states that he has never seen such a case in the 3000 patients treated in his clinic.

Norris[23] in 11,655 autopsy records of tubercular subjects found recent endocarditis in 151 cases, or 1.3 per cent. Marshall[24] thought that acute endocarditis was present in 5 per cent. of all cases of tuberculosis. Brown[25] produced experimental tuberculosis in 6 dogs, inoculating them intravenously and treating them by zomotherapy, whereupon endocarditis occurred 4 times and hemorrhagic pericarditis once. However, this same author concludes that tubercular endocarditis is very rare. The writer has not had the experience of observing such a case at North Reading. A single instance he recalls of having suspected as developing a valvular lesion at the mitral orifice a short while previous to death, but in carefully reviewing this patient's history with the help of relatives, he came to the conclusion that there was undoubtedly some cardiac defect previous to the recognized onset of his tubercular trouble.

Tessier[26] has maintained that 40 per cent. of advanced cases of pulmonary tuberculosis develop atresia or stenosis of the mitral orifice, due to the action of the toxin in the circulaing blood. However, this view is not heartily supported by other investigators, and Norris is quite skeptical as to Tessier's explanation of this phenomenon. As a matter of fact, the etiology of many of the valvular lesions was all in doubt, and but few gave any history of rheumatism or chorea or any other serious indisposition to which might be accorded the origin of the endocardial trouble. Nearly all the aortic insufficiency cases occurred in elderly people affected with arteriosclerosis.

[22] Loc. cit.
[23] Loc. cit.
[24] John Hopkins Hosp. Bull. 1905, xvi, p. 303.
[25] Amer. Jour. Med. Sci., 1903, cxxv, 1071.
[26] Cited by Norris.

Of far greater interest to me than the differential diagnosis of the various valvular lesions were the life histories leading up to the onset of lung trouble in the cardiac patients. Many instances were found of long hours worked out in poorly ventilated and dusty shops, together with a low grade state of nutrition. Some patients, especially young women, evidently had not partaken of a really substantial meal for days, and yet, suffering from overfatigue, had worked on at a gruelling occupation until tuberculosis had added the one insurmountable handicap to their endurance. The all-sufficient disadvantage of a disordered heart robbed them of whatever reserve strength they might normally have possessed.

In order to obtain greater abundance of detail on this very subject, and to carry out the investigation more to my own satisfaction, we took in hand the thorough examination of all pulmonary patients residing at one time in the Sanatorium, seeking to find those afflicted beyond all question of doubt with the complication of valvular heart disease. Then we went into the matter of their histories, comparing their lives with those of uncomplicated cases of tuberculosis, and learned that while the latter classs had pursued similarly hard occupations and were as subject to deprivation or dissipation, or both, the cardiac patients were more certainly impressed with the conditions undermining their health. That is, things of little moment to the others were of major importance to these individuals whose labor was taken always at the cost of heart fatigue and irritability. A patient with normal heart but with bilateral lung disease thought almost nothing of his former ability to work from sunrise to sunset in a damp, ill-ventilated shop, but, on the other hand, the man with antecedent heart disease often attributed his lung trouble to "overwork" and lack of nourishment. Accentuation of the many obstacles in a laboring life, together with domestic responsibilities, was apparently felt by the latter case, who perhaps would have escaped phthisical disease had his heart been sound.

Among the 183 patients examined, we found 29 cases of frank valvular heart disease; of the 183 there were 98 males and 85 females, and of the former 15 were affected and of the latter 14. That is, 15.3 per cent. of the males and 16.47 per cent. of the females examined, presented cardiac lesions. Two of these individuals, one male and one female, have not as yet been determined tubercular. Inoculations of their sputa in a series of guinea-pigs have repeatedly produced negative results, and the conclusion is now suggested that they are suffering mainly from heart disease rather than pulmonary tuberculosis. In the case of the woman slight hemorrhages are occurring from time to time, and there is pronounced mitral regurgitation, with imperfect compensatory hypertrophy of the heart muscle, but there are no definite signs in the lungs such as might indicate a tubercular process.

With the man, forty years of age, a history of syphilis with confirmatory signs and symptoms seems to account for his aortic regurgitation with a fairly well-developed compensation. No evidence of tuberculosis can at present be found in his lungs.

Therefore, it would be better to state 27 cases of pulmonary tuberculosis complicated with valvular heart disease, that is 14.75 per cent. Among the men, excluding the one probably non-tubercular case mentioned above, there were 13 cases of mitral insufficiency, including 5 cases of mitral stenosis combined with regurgitation, and 1 case of aortic regurgitation. The last case appeared in an elderly man who presented marked arteriosclerosis, which undoubtedly was the cause of his aortic insufficiency; compensation was practically nil, and he died of pulmonary tuberculosis shortly after admission.

Of the women, excluding the non-tubercular case, each of the 13 exhibited mitral regurgitation, including 2 who also had mitral stenosis.

The average age of the men affected is thirty-one years and of the women twenty-nine years, which diverges very little from the figures representing the average respective ages of all the men and all the women admitted at the Sanatorium during the hospital year 1911 to 1912. In investigating the etiological factors in the causation of their morbid conditions in this series of cases we had the advantage of "live" histories; by which is meant that the patients were present to answer whatever questions were desired regarding their former occupations and habits, whereas the information available in past histories was often lacking in certain interesting detail.

Accordingly, opportunity was offered in comparing the living regimen of our cardiac class with that of the uncomplicated. The failure of certain patients with long-standing heart disease to select proper occupations which would be more in accordance with their cardiac infirmities, and to favor their weakness in that direction, seems the cause of their succumbing to tuberculosis. It is not that they worked harder, or perhaps even so arduously as did others with sound heart, but, as a matter of fact, it is apparent that they were not competing on an even basis with normal man. The hardships of a grinding occupation were relatively greater to our cardiac patient, and in the same way, deprivation and dissipation were relatively more effective against him. Hence, his one means of escape from pulmonary tuberculosis would have been in seeking a selective occupation, and at the same time maintaining even and well-regulated habits.

The majority of the cardiac class were never told of their morbid heart condition, although they were ready to admit that they had for a long time realized something wrong with that organ. Dyspnea, especially ascending a flight of stairs, palpitation, and extraordinary

fatigue in the later hours of the day are common symptoms complained of, indicating oftentimes that the cardiac affection had existed long before the onset of tubercular disease.

One patient, a woman aged twenty-four years, worked in printing establishments for eight years previous to the discovery that her lungs were affected. While following this occupation she tried to maintain a nine- to ten-hour daily schedule in poorly ventilated dusty shops, breathing vitiated air and occasionally developing such cyanosis as to excite comment from her fellow employees. Her meals were hasty affairs, and of minimum quantity. Afternoon weariness was extreme, the patient stating that "she was ready to drop" at the closing hour; on arriving home at 7 P.M. she would be too tired to eat supper, which was the only really substantial meal provided for the day. There is sharp demarcation between the sluggish progress of her mitral disease and the sudden onset of pulmonary tuberculosis, so that it must be evident that she was not suffering all that time from incipient tuberculosis. That the soil was gradually prepared for pulmonary disease by the slowly grinding down action of an overburdened heart seems feasible.

Two young men gave nearly identical occupational histories. They were brass workers, and in their work were subjected to breathing fine metallic dust and impure air, but, as a matter of fact, could not recall a single case of consumption as having occurred among the employees of their respective shops, although all were under the same conditions. Each patient, upon examination, presented frank mitral disease as well as advanced consumption, with bilateral lung involvement. Each had noticed for several years that he became short of breath upon moderate exertion sooner than other men, and particularly that when excited his heart would beat very fast and "pound in his ears." A matter of interest was, however, their realization of becoming tired more easily than other fellow-employees and of their wornout condition as they finished their day's work.

Another pulmonary and heart case was seen in a man who for a number of years had followed the express-delivery business necessitating much running up and down stairs and heavy lifting. An excessive alcoholic habit had its inimical influence upon this man, and no doubt had as much to do in bringing on his tubercular trouble as had his strenuous occupation. However, here again was seen the sudden onset of tuberculosis which appeared as a new, clearly defined symptom-complex, superimposed on the minor manifestations of his heart trouble.

Thus did many histories of the cardiac class fall in the same category, of which those mentioned in the foregoing are fair examples. Overexertion in their daily occupations, overindulgence in excesses of a vicious nature, and lowered nutrition are the factors

conducing a lowered resistance in patients with valvular heart disease, and hence inviting tubercular infection.

Babcock[27] writes: "All authors are agreed in the declaration that nothing in the daily life of cardiac patients affects their hearts and the prognosis more disastrously than does severe and prolonged or too oft-repeated physical exertion. The day laborer who earns his daily bread by the sweat of the brow cannot be expected to keep his compensation intact for so long as will he whose vocation does not subject his heart to the possibility of overstrain."

A semiconclusion is herein suggested: namely, that individuals with valvular heart disease should know and appreciate the significance of their infirmity in order that they may choose occupations well adapted for their condition. In this manner a smaller number of such patients would contract pulmonary tuberculosis. Systematic physical examinations of factory employees by reliable clinicians must be the easier way of solving this problem, thus eliminating the pretubercular from the certainty of future infection.

Dr. Herman Vickery, of the Massachusetts General Hospital, said as he addressed a group of medical students gathered at the bedside of a cardiac patient, occupation an iceman, admitted to the hospital with disordered compensation: "Every heart case should have a certificate affirming his crippled condition, and with a notice to the public that this man, although to all outward appearances physically sound and strong, is handicapped by a serious infirmity."

With regard to the care and treatment of tuberculosis complicated with valvular heart disease we believe that we must strive and hope for not only the arrest of the tubrcular process, but also the restoration of full compensation of the heart. The heart's irritability, accentuated by the toxemia of tuberculosis, is very striking in active cases, and not until we have secured a placid condition in that organ may we hope for any improvement in the pulmonary foci of disturbance. Accordingly, I find it well to encourage my complicated case to especially avoid excitement, and to take a maximum amount of rest at proper intervals. Worry and insomnia are most prominent, and must be considered seriously by the physician who should attempt to eliminate the former by suggestive thought and pleasant distraction of the patient's mind.

We heartily agree with Babcock's[28] affirmation that no other class of cases so amply rewards intelligent and painstaking management as cardiac patients. This idea seems to apply as well to those complicated with tuberculosis, although, of course, there are more obstacles to overcome.

Medicinal treatment does not appeal at all strongly to us for this line of cases, excepting the use of digitalis and strychnine

[27] Loc. cit., p. 409.

[28] Loc. cit., p. 477.

as indicated. Depletive purgation is an effective remedy when hemorrhage occurs.

Diet is important and disordered digestion must be met with rest and proper non-irritating nourishment, rather than medication.

Intelligently precribed exercise has a very important place with this class of pulmonary patients, and should be regarded as a strong adjunct in treating the convalescent case. Only in the individual case can any advice be given on this matter; hence the uselessness of laying down any general instructions.

Finally, we wish to emphasize the need of treating the patient with every consideration which is consistent with the maintenance of firm discipline over his daily life at the sanatorium, and with the carefully guarded security of his respect for and confidence in his medical adviser.

SOME OBSERVATIONS ON THE CLASSIFICATION AND TREATMENT OF HEMOPTYSIS.

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While papers dealing with hemoptysis appear at frequent intervals in medical literature, yet we are far from having a clear underatanding of this complication from either the standpoint of its causation or treatment.

While all blood which comes from the lungs in sufficient quantities to show distinct color may be regarded as hemoptysis, yet there are different factors which cause the blood to escape from the vessels. Inasmuch as the condition which causes the escape of the blood should be taken into consideration in determining our mode of treating the hemoptysis, it is desirable to form some idea of the pathological condition which is present in and surrounding the areas from which the bleeding comes.

My study of hemoptysis is based largely on my sanatorium experience. My patients for the most part have been those well advanced in the disease. The first observation which I wish to emphasize is the fact that hemoptyses come in groups. They come at the time when the barometer is rapidly changing. At such times we nearly always have not a single one but several patients reported as "spitting blood." In our experience we have noted that foggy weather, rainy weather, as well as changes to extremely dry are all accompanied by this complication. The great majority of hemoptyses, as we find them, are slight, amounting to less than a half-ounce, although we occasionally meet quite large ones; not as large, as a rule, however, as the patients and attendants think.

According to my observation hemoptysis may be divided into the following classes:

1. A frank hemorrhage where a vessel of some size is opened and the blood flows out freely. The blood comes up into the mouth as fast as the patient can expectorate it, and in severe cases faster; occasionally causing immediate death of the patient. The blood in these cases is nearly always a bright red. The cause of this type of bleeding is the erosion of a vessel or the rupture of an aneurysm. The amount of bleeding depends on the size of the vessel involved and the extent of the rupture in its wall. This type of bleeding usually comes on suddenly, without warning, and without any previous change in symptoms. Occasionally, however, traces of blood have shown in the sputum during the day or days previous. It is the most serious of all types, and requires the greatest care in treatment.

2. A bleeding which comes on coincident with the expulsion of a necrotic mass. This type is usually preceded by several days' rise of temperature and the symptoms which accompany the increased absorption of toxins. The real cause of the bleeding in these cases is that the destructive process goes on rapidly and the wall of the abscess breaks before the vessels have been obliterated by the inflammatory process. This type of bleeding usually comes from small vessels which close quickly. At least, in my experience, it has rarely proved serious. The amount of blood lost is usually small, rarely more than a few mouthfuls at a time. This type is distinctly different from the preceding one in the way it is brought on, yet it calls for much the same treatment. Following this type of hemorrhage the patient is usually better, at least temporarily; not because of the hemorrhage, however, but because the expulsion of the tuberculous mass has given him relief.

3. A type when there is no distinct quantity of blood, but the mucus raised is mixed with color giving it a characteristic dull, pinkish color. This I consider as coming from the small vessels in the wall of a cavity. I usually consider this a sign of stimulation in the cavity, and take it to be a condition favorable to healing. This form of hemoptysis is not serious, and requires no special treatment.

4. The type of hemoptysis where the patient keeps expectorating mouthfuls of blood for several days, sometimes for weeks. There is never very much at a time, rarely more than a few mouthfuls, but this may be repeated day after day. The blood may be bright red, especially when the quantity is a half-ounce or more; or, what is more common, it is somewhat dark in appearance. I look upon this type as being due to a congestion, much the same as we see in pneumonia and heart lesions. Is it not possible, however, that it might be due to toxic action? The difficulty in this type is to recognize it. We cannot be sure of our diagnosis. This type calls

for distinctly different treatment from the types where vessels are open, but it takes a considerable amount of boldness to go against our conservative traditions. This type does not prove fatal, but serious damage seems to occur when it continues for a long time, whether the hemorrhage itself has any part in the deleterious result, or whether it is due wholly to the condition which produces it, is open to some question.

When we consider the various drugs which have been used in the treatment of hemorrhage, and take into account their supposed action on the pulmonary circulation, we must either conclude that their action is practically *nil* or that nature is able to overcome any harm that might be done by them, for the patient usually survives.

In types 1 and 2 there is a vessel open which nature closes with a clot, and there is a tendency for bleeding to continue until the opening is firmly closed. It is imperative to retain the clot in the opening until it has organized and sealed the vessel. To this end everything must be done that will quiet the circulatory system. Both mental and physical rest should be insisted upon. The mental rest can oftentimes be obtained through reassuring the patient and giving him confidence and hope. Where this cannot be done, a hypodermic injection of morphine is to be resorted to. Personally, I do not like to use morphine when I can avoid it, yet at the same time it meets two important indications in the treatment of hemorrhage: (1) it quiets the patient, and (2) it reduces the tendency to cough. When I do resort to morphine I rarely give a large dose, but usually employ $\frac{1}{16}$ grain hypodermically. This small dose seems to have a decidedly sedative action and avoids the severer blunting effect on the nerve endings of the respiratory tract, which follows larger doses. I feel that great harm is often done in the treatment of hemorrhage by large and repeated doses of morphine. It prevents the patient clearing out the blood from the respiratory tract, and thus favors a complicating pneumonia.

For the maintenance of physical rest the patient should be put to bed in a comfortable position, usually on his back, with shoulders a little high; and, if the bleeding has been severe, no movement should be allowed. During the first twenty-four hours, as a rule, he becomes tired of the position, but after that he lies with comparatively little discomfort. He should be kept quiet until all danger of recurrence has disappeared. After there has been no further bleeding for twenty-four hours, the nurse should change his position by rolling him over on his side and holding him there with a pillow. He should not be allowed to sit up in bed until all color has disappeared from the sputum for at least three days. Of course, where the hemorrhage is slight such stringent regulations are not necessary, but in a severe hemorrhage, these measures are often life-saving.

In way of medication, as a rule, reliance should be placed upon

tincture of veratrum viridi, giving five drops every three hours until the pulse slows, then reducing the dose to four drops or three drops every four or five hours. The veratrum is somewhat slow in its action, and in order to get an immediate effect, we use nitroglycerin, $\frac{1}{100}$ to $\frac{1}{50}$ grain, dissolved on the patient's tongue. A hypodermic tablet of nitroglycerine dissolved on the tongue will produce an effect in a few minutes, and then by the time its action is passing off the veratrum is beginning to show its effect.

Recently we have been trying pituitrin in some of these cases. It seems to promise well as far as we have observed it. It has been shown to raise systemic blood-pressure and lower that of the pulmonary circulation. In several patients treated with it the bleeding seemed to stop more promptly than is usually the case. Another action which we noticed in 2 cases was an evacuation of the bowels within a few moments after the remedy was absorbed. We have employed it in doses of $\frac{1}{2}$ to 1 c.c., repeated in four hours.

Artificial pneumothorax is often valuable in types 1 and 2.

For that type of hemoptysis which we have designated as "congestive," mentioned as type 4, we would use a different line of treatment. It is difficult at first to be sure that a hemoptysis belongs to this type; in fact, it is necessary to study a case for a few days, as a rule, before this can be determined definitely; and we think it is safest to treat every case at first as though it were an open vessel. If it is of the congestive or toxic type, it is apt to be prolonged, the spitting of blood will continue for quite a little time, not in large quantities but small quantities each day, and numerous times during the day. We keep the patient, suffering from this type, quiet, just the same as those suffering from the other types, but instead of using veratrum and nitroglycerin, we use some circulatory stimulant. These are the cases that we think obtain decided benefit from the adrenal preparations. Digitalis also works well at times and we also feel that strychnine is sometimes of decided benefit.

There are numerous complications associated with hemorrhage which require some attention. They are not well understood, and are not always easy to handle. We often see a marked shock following a hemorrhage, even although the amount of blood lost is small; and there are times when it seems that respiratory failure is threatened. Under such conditions we have felt in one or two instances that the life was probably saved by the use of strychnine. Two complications that are not uncommon in hemorrhage are paralysis or paresis of the bladder and of the bowel. Obstinate constipation follows a hemorrhage in many instances, and the strange thing is that ordinary cathartics in these cases fail to act. In several severe hemorrhages we have seen it necessary to remove the feces from the bowel mechanically. After experimenting a great deal with various laxatives in these cases we have found that the rhubarb pill seems to act the best of all remedies. In these cases

we give 5 grains of rhubarb, three or four times a day, and in most instances it seems to act well. We have also seen a few cases where it was necessary to catheterize the patient following hemorrhage.

The question has often been discussed as to the harm or benefit arising from hemorrhage. We do not believe that hemorrhage, *per se*, ever does the patient any good, although we have seen numerous instances where the patient improved following the hemorrhage. This was not on account of the hemorrhage, however, but because of the fact that the hemorrhage was due to the rupture and expulsion of a necrotic mass, as a result of which the patient was relieved of toxic symptoms. The second type of hemorrhage mentioned is often followed by an improvement in the condition of the patient. The following case illustrates this point:

T. W., aged forty-eight years, suffering from active process in the lung. Was running high temperature, as high as 103°, with severe intoxication, mental and physical depression, night sweats, and severe prostration. An abscess formed in the lung. His sputum increased markedly, and the increase was accompanied by a hemorrhage. The temperature dropped considerably and gave the patient relief. A few days later the abscess opened freely and a large quantity of pus was poured out, giving complete relief from temperature and toxemia. The hemorrhage did not cause the amelioration of symptoms, but the rupture of the abscess did.

Hemorrhage may be harmful in several ways. Following the opening of a vessel, bacilli may escape into the blood-stream and cause a dissemination of the disease. We have seen several instances where an acute disseminated tuberculosis followed hemorrhage.

Another common complication which often proves harmful is an accompanying pneumonia. From the blood which trickles down into the lung an irritation is set up and pneumonia results, which, in some instances, leaves considerable damage after it has finally subsided.

A CASE OF CONGENITAL ABSENCE OF THE LOWER HALF OF THE INTERAURICULAR SEPTUM.

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Malformations of the septa of the heart, while not common, are not unique. There are, in all probability, many more cases of potentially patent foramen ovale than are ever diagnosed or even suspected, owing to the absence of symptoms, which autopsy readily explains in showing the defect to be due to the non-union of overlapping edges of the foramen which the pressure of the blood keeps

tightly in apposition, the foramen thereby being functionally, if not anatomically, closed.

The case herewith reported derives its particular interest, not alone from the extent of the defect, but more from the complete absence of any symptoms referable to the condition which was found at autopsy.

Theoretically, a lesion so extensive and of so functionally important a character should have given rise to grave and significant symptoms, and markedly affected both the health and the general development of the individual; in spite of the fact, however, that the case was under treatment essentially for cardiac defects and that particular care was, therefore, directed toward the heart and all symptoms referable to it, no suspicion of the existing abnormality was aroused in any way.

The clinical history was as follows:

Florence A., aged eighteen years, was admitted to the University Hospital on January 25, 1913, for dyspnea, palpitation, and pain in the right knee. The history, taken shortly after admission, was as follows:

History of Present Illness. So far as she can remember the patient has always been prone to dyspnea and palpitation on moderate exertion, but never, until the present attack, to such a degree as to arouse her apprehension or specifically direct her attention to it.

About January 1, 1913, she began to have severe headaches, accompanied by constant backache, dyspnea, and palpitation, these latter being so pronounced at times as to preclude sleep. There is no history of precordial pain during these attacks.

January 24 she had severe, sharp pains in her right knee, but does not know whether it also became red or swollen. She was admitted to the hospital the following day, and within the next few days, in the order cited, the pain spread to her right foot, right hand, right elbow, and right shoulder, the parts becoming red and swollen, as well as painful; within the next week her left foot and left knee were attacked in the same manner.

Her dyspnea, she thinks, has not become ncticeably increased, but she is conscious at times of a rather marked palpitation. She has never at any time had any swelling of the feet other than that just mentioned, nor has there ever been any puffiness of the face.

She complains that, occasionally, and especially since she has been in the hospital, she sweats at night, but gives no history of previous night sweats nor constant cough. Since admission she has had a slight, spasmodic cough, which she attributes to "throat irritation," and which is accompanied by some slight morning expectoration of whitish mucus.

Her appetite, until recently, has always been good and her bowels regular. At times she has had attacks of "indigestion," accompanied

by gaseous distention to such a degree that she is unable to wear corsets, but these attacks seem to be associated with dietetic errors, and questioning fails to elicit anything which would point to the abdominal distention being in any way ascitic in character.

She gives no history of other disorders other than the menstrual history given below.

Past Medical History. Measles, parotitis, varicella, and scarlatina in childhood; later influenza and frequent attacks of tonsillitis. No history of chorea, pneumonia, typhoid fever, nor rheumatism other than the present attack.

Until she was nine years of age she was a somnambulist; always had vivid dreams, and talked in her sleep, the two latter conditions being still present to a somewhat lessened degree. Beyond the attacks of "indigestion," cited above, there is no history of gastrointestinal disturbance.

Menstrual History. The menses began when thirteen years of age, when she was confined to her bed for three weeks before their appearance. They have always been painful for the first two or three days, and the flow, when established, lasts, as a rule, for five or six days. She is irregular, often missing for a time, the last period not appearing until twelve weeks after the preceding one, lasting for a week, and then after the intermission of a week, again appearing for another week.

She contracts colds easily in the winter, but says they are not of long duration.

While always, she says, "inclined to be delicate," she gives no history of specific complaint, and says she was in her usual condition of health until January, 1912, when, while on a visit to Wyoming, she contracted an attack of "la grippe," which confined her to bed for two weeks, at times with a temperature of 106°, and from which she did not sufficiently convalesce to be able to travel until one month after its inception.

From the following February until June she felt about as well as usual; by this she means that she was conscious of no subjective symptoms other than moderate dyspnea on exertion, and then only to what she considered a normal degree, and had no specific complaints; but in June she began to feel languid and tired, lost her appetite, and was attacked with severe frontal, occipital, and parietal headaches, together with dyspnea and palpitation, sufficiently marked to lead her to consult a physician, who told her that she had "cardiac trouble."

Under treatment she improved perceptibly, the palpitation and dyspnea becoming negligible, and she was not particularly ill, although consulting her doctor once or twice a month, until the day after Thanksgiving, when she again had a slight attack of what she called "la grippe," which kept her in bed for two days. On her recovery from this illness she felt languid, tired, and without

energy until Christmas, when, for a short time, she felt better. Shortly after this date, however, her dyspnea again began to become troublesome, and she developed acute inflammation in her knee, and from this point on the story is taken up in the history of her present illness.

Family History. Negative.

Physical Examination. The patient is a rather slender, pale, and delicate-looking white girl of nervous, high-strung appearance, giving no external evidence of pain nor marked dyspnea.

The skin is fair and clear, the eyes bright, and the cheeks flushed, due, in part, to dilatation of the finer capillaries, which are plainly seen through the skin; fine, bluish veins are also seen over the temples and in the neck. Of small frame, the general nutrition is fair, and there is no evidence of recent emaciation.

The general appearance is that of a young girl underdeveloped physically and younger looking than her age, of a rather infantile type in appearance.

There are no gross abnormalities of the head or face.

There is some slight play of the alæ with respiration, more so than is accounted for by the degree of dyspnea present at this time.

The lips are dry, slightly scaly, and pale. The eyes are bright, with equal pupils reacting normally to light, convergence, and accommodation; the sclera are clear.

The neck is rather slender, and the superficial veins are clearly seen through the skin, and on each side there is a marked systolic pulsation in the larger vessels.

The throat is negative; the mucous membranes are much paler than normal; the tongue is coated with a brownish fur, approaching closely to the edges; the teeth are well formed and in good condition, though there is a slight degree of pyorrhea, and the gums are also paler than normal.

The hands are small and slender, with a slight tendency toward broadening at the ends of the fingers, and a slight cyanosis of the nail-beds. The right hand is swathed in bandages and gauze, and the fingers, when exposed, are very slightly swollen, slightly reddened, hot to the touch, but not markedly tender nor painful except on semiflexion.

There are no masses nor roughenings over the tendons, no bone tenderness, and no apparent joint effusions of marked degree. There are no glandular enlargements in either the elbow or axilla.

Both knees and feet are wrapped in gauze and bandages; there is, however, no limitation of motion nor tenderness on handling; the affected parts are not conspicuously red nor swollen, and there is no edema over the tibia.

Thorax. The skin is fair and clear, moist, and warm, with no marked eruptions nor gross abnormalities. The superficial veins are easily seen, though not markedly dilated.

The chest is well-formed and of fair development, and although the patient is not of muscular nor adipose build, there is no apparent evidence of loss of weight; the ribs, however, while not prominent, are clearly outlined beneath the flesh.

There are no gross abnormalities of the bony frame-work suggestive of rickets or other like condition.

The breasts are of moderate size and normal in shape, but slightly underdeveloped, with large nipples but no apparent areola.

Expansion is fair and equal on both sides. The accessory muscles of respiration are not markedly active, and there are no marked supraclavicular or infraclavicular depressions. There is an evident systolic pulsation in the costal angle, and, in the region of the apex, a diffuse, heaving impulse is plainly visible.

Lungs. Anteriorly the percussion note is normal, with the exception of a suggestion of hyperresonance at the apices; there are no areas of dulness. Both tactile fremitus and vocal resonance seem slightly increased at the apices, and down to about the fourth rib. The breath sounds are rapid, slightly harsh, and inspiration is loud. There are no rales. Posteriorly the percussion note is normal, but tactile fremitus and vocal resonance are slightly increased throughout. The breath-sounds are slightly harsh, and tend somewhat toward a tubular character at the bases; inspiration is prolonged, and on the left side about the angle of the scapula a few creaking rales are heard, but not constantly.

Heart. Upper border, third rib; right base, 5 cm.; left base, 11.5 cm.; right oblique, 9.5 cm.; left oblique, 14.5 cm.; height, 8.5 cm.

On admission the apex-beat was diffuse, and was quite close to the midaxillary line; there was a marked gallop rhythm, and the heart was so rapid that it was difficult to time the murmurs, of which there were several present: a harsh, presystolic murmur at the apex, merging into the first sound, and a suggestion of a diastolic murmur at the aortic area. The pulmonic first sound was harsh and murmurish, the pulmonic second much accentuated and slapping.

Later, when the heart had quieted somewhat, a more thorough examination was possible and revealed the following conditions:

At this examination, four days after admission, the apex beat was situated 3 cm. outside the nipple line, and presented a somewhat heaving, diffuse impulse; there was also a suggestion of a thrill at this area.

The heart measurements at this time were as follows:

Upper border, third rib; right base, 2.3 cm.; left base, 11 cm.; right oblique, 13 cm.; left oblique, 14 cm.

At the mitral area there is a double murmur: a somewhat harsh, systolic murmur, long and blowing, and a soft, purring, diastolic murmur. The sounds are slappy and forcible.

The murmurs, especially the systolic, are transmitted into the

axilla, and are well heard as far out as the axillary line; here they become somewhat fainter and begin to diminish in intensity, while the heart sounds become more clear, until, at the angle of the left scapula, the murmurs are lost while the heart sounds are well heard, both forcible and slappy, the second sound markedly accentuated.

Over the tricuspid area the same murmurs are heard, although not so loudly, and the sounds are transmitted for a short distance up the sternum. It is not clear at this examination whether the sounds heard at the tricuspid area are transmitted from the mitral area or whether there is, in addition, a tricuspid lesion; the latter seems slightly more probable.

Over the aorta there is a distinct systolic thrill, and, on auscultation, a harsh, systolic murmur and a blowing diastolic murmur, which are transmitted upward into the vessels of the neck, loud over the carotids, fainter in the vessels of the neck itself.

The pulmonic second sound is strongly accentuated, but auscultation of this area reveals no other abnormalities.

Abdomen. The abdomen is of normal shape, size, and conformation, and presents no gross evidences of swellings nor tumor masses. There are no eruptions, the skin is clear, and there are no marked engorgements of the superficial veins.

The abdominal wall is relaxed and the skin is warm and moist. There is an evident epigastric pulsation.

The stomach does not appear to be markedly distended nor ptosed so far as can be ascertained through percussion; peristalsis is active, and there appears to be a moderate amount of gas present.

The liver extends from the sixth rib to 5 cm. below the costal margin, and on percussion is slightly tender. The spleen and kidneys are not palpable.

The inguinal glands are not enlarged, and there are no herniæ present.

No pelvic masses nor tenderness can be demonstrated.

Temperature, 99°; pulse, 100; respirations, 36.

Blood. Hemoglobin, 70 per cent.; red-blood cells, 3,680,000; white-blood cells, 16,400; polymorphonulcear, 72 per cent.; lymphocytes, 27 per cent.; large mononuclears, 1 per cent.

Urine. Amount, 500 c.c.; color: dark amber, cloudy, nebular sediment; specific gravity, 1.030; reaction, acid; albumin, light cloud (ferrocyanide test); sugar, none; sediment: no casts, cylindroids, nor red-blood cells; a little mucus, a few leukocytes and epithelial cells; no crystals.

Blood-pressure: Systolic, 94 mm.; diastolic, 62 mm.

Such was the condition of the patient when first seen by me, and on the above findings a diagnosis was made of acute, infectious arthritis complicated by an acute exacerbation of a chronic endocarditis, and treatment was instituted accordingly.

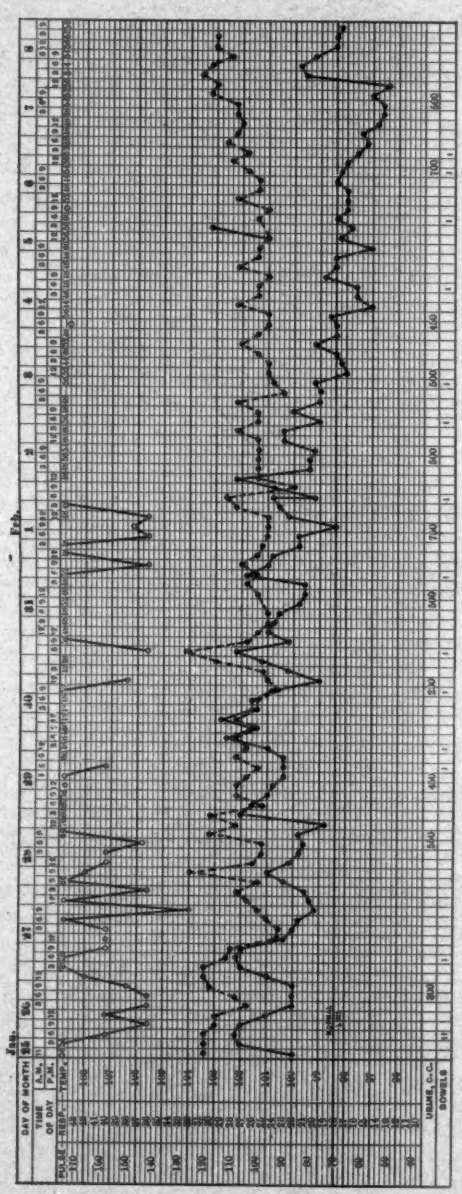

FIG. 1.—Clinical chart: O——O = respirations. ●- - -● = pulse rate. ●——● = temperature.

A double mitral insufficiency, due to a preceding endocarditis, was readily diagnosed on the history and character and constancy of the findings in this area, as was also an aortic stenosis. The tricuspid murmurs, however, were for some time the subject of discussion, so confusing were the shifting murmurs, due to the acute process, and the transmission of those due to the mitral lesion; eventually a tentative diagnosis of a more moderate grade of tricuspid stenosis was adopted.

The course of the disease was, at first, uneventful and presented about the usual condition of affairs to be expected of such a condition, as may be seen from the attached temperature chart and clinical record. Three days after admission some skodaic resonance and bronchophony were noted over the left base posteriorly, and six days after admission a capillary pulse was observed. The size of the liver was subject to some fluctuation, though never reaching normal, and at no time was the temperature very high. It is of great interest to note that at no time until the end, despite the high respiration rate which was a feature of the case and significant of the marked cardiac embarrassment, was there any cyanosis of sufficient moment to be noted on the daily records.

Shortly, however, an increasing leukocytosis became a marked feature of the blood examination, the count rising as high as 24,400; the dyspnea began to increase, the patient became toxic, restless, and distressed, especially at night, and a drop of temperature with a rapid pulse became a noticeable feature of the night records. In reference to this latter feature, it may be remarked that this was probably an incorrect record; the temperature was taken by mouth and the low levels were in all probability largely due to marked dyspnea and the consequent passage of large amounts of air over the bulb of the thermometer.

On the thirteenth day after admission there was a decided change in the condition, the following note being recorded:

"On entering the ward today the patient is lying on her right side, evidently dyspneic, the movements of the chest, alæ of the nose, and accessory muscles of respiration being distinct, and is evidently not as well as yesterday.

"When turned on her back she complains, becomes perceptibly uncomfortable, and pronouncedly more dyspneic than before, the respirations going to fifty-six per minute.

"She is restless, says she does not feel good, and complains of 'hot flashes,' and that she did not sleep well. The chart records a steady fall of temperature during the night, to 96.8, from which this morning there has been no recovery. The respiration rate is 54, and the pulse 124 per minute.

"Her position and condition attracted attention to her lungs, and, on examination, there was found a marked dulness of the upper right lobe, while over the entire left lung, both anteriorly

and posteriorly, the note is about normal. In the right upper lobe anteriorly and throughout there are many rales, and the breath-sounds are bronchial in type; there are comparatively few rales in the left lung, mainly at the base, and the breath sounds are not so decidedly bronchial.

"Diagnosis is made of lobar pneumonia of the right upper lobe.

"The pulse is rapid, and there is a gallop rhythm at the apex, the apical impulse being diffuse and heaving. The mitral murmur is fainter today; the sounds at the aortic area remain about the same as yesterday (no murmur at that time, but the sounds are very slappy and accentuated)."

In spite of attempts to stimulate the heart and improve the general condition, there was no marked improvement, and the subsequent course of the case was as follows:

Later in the same afternoon the patient became markedly cyanotic and dyspneic, the heart extremely irregular in action, and the general condition poor. She was bled sixteen ounces from the arm, and oxygen was administered, with decided improvement, which, however, as after-events showed, was only temporary. At this time her temperature by mouth was 96° and by rectum 99.2°. A similar attack occurred later in the evening, which was relieved to some extent by the administration of oxygen, heart stimulants, venesection, and saline infusion; but from midnight on her condition grew steadily worse, and she became more and more cyanotic, with marked palpitation, cardiac irregularity, and dyspnea, and death occurred at 8 A.M. the following morning.

Permission was obtained for a limited autopsy, the express condition being that all of the tissues and organs be replaced.

The autopsy, which was performed by Dr. K. M. Lynch, of the pathological department, is briefly abstracted below:

Autopsy 4081–13–6, F. A., Body of a young white woman, well formed and well preserved; about 5 feet four inches in height. Rigor mortis slight; livor mortis fairly well marked over dependent portions of the body. Skin white and dry; mammary glands fairly well developed. External surface of the body in good condition.

Abdominal cavity contains about 200 to 300 c.c. of clear fluid. Membrane smooth and glistening. The liver extends about three fingers' breadths below the costal margin across the midline. Mesenteric lymph nodes enlarged, hard, and calcified; probably tuberculous.

Spleen: Small, firm, cuts with increased resistance, and on section is of a dark, blue-red, slaty color, and shows slaty induration and a chronic passive congestion.

Kidneys: Right weighs 140 grams, the left 130 grams. Capsule slightly adherent; on section shows cyanotic induration; ureters patulous.

Liver: The liver weighs 140 grams, and is slightly enlarged for

the size of the individual. The organ is flabby, cuts with leathery firmness, surfaces smooth and capsule transparent, and on section shows a mottled red and white appearance, the white areas being areas of degeneration and the red areas of congestion; vessels all enlarged and contain dark red blood; there is a rough, granular, retracted condition of the cut surface, which is decidedly firm. The organ shows parenchymatous degeneration, passive congestion, and early cirrhosis of the cardiac type.

The above is a brief extract of the more prominent gross findings in the more important abdominal organs, the features of most interest being noted in the chest, the examination of which follows in full:

Thorax: On opening the breastplate the whole anterior portion of the chest is apparently filled with the heart. It extends from about the upper border of the sternum downward on the right to the junction of the cartilage and the bone, over to the left with a blunt apex outside the nipple line, and almost to the axillary line at the sixth rib. The pleural cavities are both free from fluid or adhesions; both lungs are collapsed somewhat in the posterior portion of the cavities; membranes smooth and glistening.

Pericardium: The pericardium shows a smooth, glistening membrane, and contains several excessive centimeters of clear, straw-colored fluid. As the heart lies, the whole anterior surface is formed by the right heart. The pulmonary artery is much enlarged, the aorta very small.

Heart: The organ is some three or four times the size of the normal heart for this sized individual. It is of somewhat rounded, blunt-pointed shape; the majority is formed of the right side of the heart. The surface is smooth, and there is very little subpericardial tissue.

Incision into the different cavities reveals but little fluid blood, the right side of the heart being filled with a large mass of firm chicken-fat clot, while the left side contains a small amount of chicken fat and quite a large currant-jelly clot. The lowest portion of both ventricles contains a decidedly black-colored clot of the muratic variety.

The organ, when emptied, weighs 570 grams. It is decidedly flabby, the myocardium being rather pale, with decreased consistence. The right ventricular wall measures an average of 1 mm. in width, the right auricular wall an average of from 2 to 7 mm. in width. The papillary muscles of both cavities show an enormous increase in size.

The wall of the left ventricle averages 9 mm. in width, the left auricle from 1 to 4 mm. in width. The walls of these cavities are decidedly firmer and redder than on the right, and the papillary muscles show no distinct increase in size. The cavities of both auricles and of the right ventricle are decidedly enlarged; that of the left ventricle but little enlarged.

The mitral valve leaflets are decidedly thickened, retracted and adherent to each other at the ends. The orifice measures 2.5 cm. in its long diameter, and when split, 1.5 cm. in width. The valve leaflets are unusually abundant with large thick chordæ tendineæ extending even up to the base of the leaflets.

The aortic orifice measures 4.5 cm. in circumference, and is extremely small, hardly admitting the index finger; the valve leaflets are in good condition and the aorta enlarged somewhat beyond the aortic ring, but is never as large as it should be. Its intima is smooth and glistening, and the wall is elastic.

The tricuspid orifice measures 13.5 cm. in circumference. The leaflets are about the normal length, thin and translucent. The pulmonary artery throughout its entire length is decidedly much too large.

The wall, however, is about normal in appearance, elastic, and with a smooth, yellowish-white intima.

At the line of closure on the auricular side of the mitral valve leaflets there is a decided line of yellowish-white or reddish-white, small, fibrinous vegetations.

Both auricles, or rather what should be both auricles, are very much dilated, especially the right, which is also distinctly hypertrophied. The papillary muscles are larger than those ordinarily seen on the wall of the left ventricle.

These two cavities are merely separated from each other by a thin, semilunar flap of endocardial tissue extending from the roof in a half-moon shape down into the cavity, thus leaving an opening between the two auricles, measuring, without stretching at all, 3 cm. in diameter, which is well rounded; on the floor of the cavity, formed by the two auricles, there is no septum whatever.

The mitral orifices naturally come close together, and the bases of their valves are only separated by a matter of 2 to 3 cm.

In the thin, semilunar partition between the two auricles and the roof are two smaller openings, one about 2 mm. in diameter, and one about 4 mm. in diameter, the larger one being about the position and about the shape and size of a patulous foramen ovale. It has a flap of endocardial tissue coming down over it like a functionally closed foramen ovale. There are no evidences of inflammatory trouble around either of these openings, and all are apparently congenital.

The figure following is a diagrammatic representation of the conditions found in the heart, representing these as seen in a sagittal section of the organ.

The discovery of such an extensive cardiac lesion was an entirely unsuspected factor in the case, and in view of the entire absence

of any indication of congenital abnormality, aroused great interest and opened up a wide field of speculation in search of some explanation of the apparent functional compensation which had taken place.

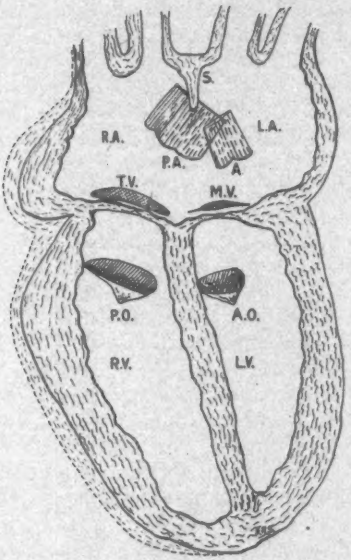

FIG. 2.—Diagrammatic drawing of conditions found in the heart.

			Normal.
Weight	570 gms.		250 grams.
Right ventricular wall diameter	1 cm.		4 mm.
Right auricular wall diameter	2–7 mm.		2 mm.
Left ventricular wall diameter	9 mm.		9 mm.
Left auricular wall diameter	2–4 mm.		2 mm.
Mitral orifice	2.5 cm. long. 1.5 cm. wide.	circumference:	9 cm.
Aortic orifice	4.5 cm. circumference.		8 cm.
Tricuspid orifice	13.5 cm. circumference.		11 cm.
Pulmonary orifice	10.0 cm. circumference.		7 cm.

R. A.	Right auricle.	P. A.	Pulmonary artery.
L. A.	Left auricle.	A.	Aorta.
R. V.	Right ventricle.	T. V.	Tricuspid valve.
L. V.	Left ventricle.	M. V.	Mitral valve.
S.	Septum.	A. O.	Aortic orifice.
P. O.	Pulmonary orifice.		

The question first presenting itself was, naturally, whether or not the condition was congenital or had been acquired in late life, and this leads to a brief review of the development of the heart insofar as we are enabled to elaborate it from a study of comparative anatomy.

Starting as a result of the fusion of the two primitive vessels, with a simple tube, fairly straight and of fairly uniform caliber, changes in form and in the relative position of its various parts soon take place. It soon becomes irregularly enlarged and a series of four dilatations with intervening constrictions are distinguishable; these dilatations, from behind forward, are (*a*) the sinus venosus, (*b*) the auricle, (*c*) the ventricle, and (*d*) the bulbus arteriosus. The short constriction between the auricle and the ventricle is known as the auricular canal. Meanwhile an elongation and bending of the tube takes place, resulting in the formation of a U-shaped loop, the posterior or venous end lying to the left and above. Subsequently the auricle ascends behind the ventricle.

While these changes have been taking place, the division of the heart cavity into its permanent chambers commences, the separation of the auricles being the point of particular interest in connection with this case. This occurs through the growth of a septum and through the thickening and fusion of the middle portion of the auricular canal, these thickenings being termed the endocardial cushions. The separation of the primitive auricle into right and left portions is indicated by the appearance of a groove on the upper and posterior wall, opposite which an auricular septum grows downward into the interior of the auricle. Its lower border gradually approaches the endocardial cushion in the auricular canal, and, for a time, a small opening is left between the upper end of the endocardial cushion and the lower end of the septum. This is the ostium primum, which later is closed by the fusion of the cushion with the septum, but before its closure is completed, an aperture appears in the upper part of the septum; this latter aperture, the ostium secundum, becomes the foramen ovale. A second auricular septum, the septum secundum, grows downward to the right of the first; its lower margin grows downward past the foramen ovale, but stops some distance from the posterior wall of the auricle, and, after birth, through fusion with the first, closes the foramen.

Applying these facts to the case at hand, we note, first of all, the absence of any sign of inflammatory trouble either in the flap-like partition itself or in the openings in its wall; further, the destruction and absorption of such a large amount of tissue as would be necessary to produce a like condition is manifestly improbable, if not incompatible, with existence; certainly, it could not have occurred without the signs of a grave illness, any mention of which is not found in the medical history of the patient.

Were it not for the opening so closely resembling in size and position, as well as in appearance, the foramen ovale as seen in the normal interauricular septum, the thought would occur that the condition was due to an absence of the interauricular septum as a whole and its representation by the persistance of the normally transitory septum spurium which, in the embryo, grows downward

from the roof of the auricle and is continuous with the right and left halves of the sinus venosus. The presence of the foramen ovale, however, or what closely resembles it, normally closed off by an overlying endocardial flap, forces the conclusion that the condition was due to a cessation of development and growth downward of the two interauricular septa which never reached, and consequently never fused, with the endocardial cushions. How to explain this lack of growth, affecting both septa, is, of course, a matter for purely hypothetical speculation, and, while it is recognized that a fetal endocarditis may occur and is not an uncommon cause of congenital septal defects, indications of such a condition are not demonstrable in this case and do not appear probable.

Of more interest is the explanation, if possible, of the functional compensation which apparently took place in this individual.

The comparatively normal growth and development of the patient is evidence, *per se*, that the cardiac defect occasioned no trouble during her intra-uterine existence; this is readily explainable when the peculiarities of the fetal circulation are recalled.

Normally, in the fetus, the blood entering the right auricle, is guided by the Eustachian valve through th foramen ovale into the left auricle where it becomes mixed with a small amount of blood returned from the lungs by the pulmonary veins; from the left auricle it passes into the left ventricle and thence to the aorta to gain the systemic circulation. In this individual the absence of the interauricular septum merely replaced the normal fetal condition in allowing a free communication between the auricles. At birth, however, a marked change takes place and the conditions in this case became at once extremely abnormal.

Normally, when respiration is established, an increased amount of blood from the pulmonary artery passes through the lungs which now perform their office as respiratory organs. Almost immediately after birth the foramen ovale is closed by the apposition of the valvular edge of the septum secundum against the annulis ovalis, the continued contact being due to respiration which increases the pressure in the left auricle, fusion and closure normally occurring about the tenth day after birth.

In this individual, however, no such condition obtained, and there remained, anatomically, a large area of wide and free communication between the auricles permitting, and, indeed, necessitating, an intimate mixture of venous and arterial blood.

The immediate result of such a condition is cyanosis and of an extreme grade, and it may be remarked, in passing, that in no class of ambulatory cases is cyanosis so pronounced and extreme as in those of congenital heart disease. The familiar "blue baby" is a striking example of the effects of a relatively moderate mixture of venous and arterial blood, an example with the picture and the results of which everyone is familiar; here, however, was an indi-

vidual in whom there should have been practically an absolute mixture of the two streams, and who, notwithstanding, was not a "blue baby," was never cyanosed, was never, until almost sixteen years after her birth, conscious of any cardiac abnormality of function, who exhibited no outward sign of failing or weakened circulation, who presented no clubbing of the fingers or toes, who evidenced no sign of marked physical or mental lack of development, who led a normal though probably quiet life, who contracted, in addition, valvular lesions, adding to the embarrassment of the heart, and who, nevertheless, died at the age of eighteen from an intercurrent infection with her congenital malformation entirely unsuspected.

How is this to be explained? The conclusion is almost unavoidable that functionally the defect did not exist, that it was in some manner entirely compensated. The assumption is born out by several facts which are noted in the examination of the heart itself.

In the first place there was a marked hypertrophy of the wall of what should have been the right auricle, while the wall of the left auricle was not correspondingly developed. Unless these two cavities were, during life, separated from one another to some extent, and capable of acting as separate compartments, hypertrophy of the wall of one could not very well occur without hypertrophy of the wall of the other. Again, the fact that the foramen ovale, or what apparently represented it in the remnant of the interauricular septum, was normally closed by the fusion of the overlying, valve-like flap of endocardial tissue is evidence that more or less pressure was exerted on these two surfaces to keep them in apposition; normally this is due to the higher pressure in the left auricle due to respiration, and, since fusion occured in this case, there was probably such an increased pressure in the left auricle which must, therefore, have acted as a separate chamber. Thirdly, and what is most striking because it is fact and not speculative, there is the absence of any symptoms of imperfect oxygenation of the arterial stream which must have occurred unless, by some manner, the right auricular chamber was shut off—at least to a great extent—from the left. It seems justifiable, therefore, in fact, almost unavoidable, to assume that such a separation into independent chambers acting independently did take place; the possible mechanism by which it might have occurred will be noted later, when it will be seen that, while accounting for the hypertrophy to some extent, and for the closure of the foramen, it cannot, however, be adduced as the main or only factor in the functional compensation.

The case, as a whole, presents many interesting features, but perhaps the most striking is the entire absence of cyanosis, even a slight degree of which, as the patient was a pronounced blonde, with a fair and clear complexion, would have been at once evident.

There are several theories on which this might be explained: First, on the supposition that the two auricles were functionally, if not anatomically, separated, and that contamination of the arterial with the venous blood occurred only to a slight degree; the mechanism of such an occurrence, however, and exactly how it could have occurred in the presence of such conditions as were found so as to prevent the mixture of the two streams, we are unable to conceive or explain. The closing off of the two chambers is conceivable by some such mechanism as the following: with each contraction of the auricles the fringe representing the septum necessarily approached to a lesser or greater degree the floor of the auricles. Assuming a contraction of sufficient force, we could imagine the approximation of the fringe and the auricular floor, thus shutting off the two chambers and making of them functionally separate cavities. This, however, does not satisfactorily explain the lack of cyanosis, because such an approximation would necessarily have to occur when the auricles were emptying themselves of blood; immediately following there occurs auricular diastole, when the blood flows in from the venæ cavæ and the pulmonary veins into the two chambers, and the auricles are relaxed. If they are relaxed the septum would not be completed and the mixture of blood would, therefore, take place, the separation into separate compartments taking place in auricular systole when the two streams were already contaminated.

Another supposition, looking at the case from another viewpoint, may be elaborated as follows: In cases of patent foramen ovale, while a certain amount of leakage takes place at the midpart of the auricular diastole when the level of the inflowing blood reaches the opening of the foramen, the major portion of the contamination of the arterial chambers with venous blood from the right auricle takes place at the moment of auricular contraction, when the blood, taking the path of least resistance, is forced through the patent foramen; remembering the short interval between auricular diastole and systole, we may assume that, as the arterial blood flows into the left auricle, part of it, owing to the sclerotic condition of the insufficient mitral valve, falls at once into the left ventricle; the remainder is forced into the left ventricle before an intimate admixture with the venous blood of the right auricle has taken place, and, therefore, enters the systemic circulation with only a minimal amount of contamination. This would be further aided by the functional separation of the two chambers as above suggested.

Both of these suppositions are, necessarily, somewhat farfetched, improbable, and weak; the fact remains, however, that compensation of some kind did take place, and, if we cannot assume such an explanation as the foregoing, we are forced to the theory that the pulmonary circulation was always more extensive than the sys-

temic, and was thus enabled to cope with the problem of the excessive aëration necessary to maintain a proportion between the contaminated blood stream of the systemic circulation and the necessities of the tissues.

The examination of the heart apparently furnishes ample evidence upon which to base such a theory.

In the first place, both the right ventricular and right auricular cavities were much dilated. That this was not due to the terminal dilatation of cardiac failure consequent upon the pneumonia and other embarrassment under which the patient labored is evidenced by the marked hypertrophy which is present in the walls of both cavities, showing the condition to have been one of gradual development and long standing, and we have, therefore, in these two factors, the dilatation showing that the chambers contained more than the usual amount of blood, and the hypertrophy evidencing increased work, extremely suggestive indications of an increased amount of blood in the pulmonary circulation. Add to this the marked enlargement of the pulmonary artery and the links in the chain are apparently complete; as this vessel plays but little part in the fetal circulation and only becomes active after birth and the inception of the respiratory function, it must be looked upon as a condition developing after birth and with the growth of the individual.

It may be objected that all of these factors, with the exception of the hyperplasia of the pulmonary artery, might be accounted for as the end-results of the mitral stenosis which was present. It is true that the mitral valve was markedly stenosed and thus offered an obstacle to the passage of any large—we might say the normal—amount of blood; on the other hand, however, the aorta was extremely small, approximately only half as large as normal, and, therefore, was not capable of accommodating any more blood than the amount which the small mitral orifice was capable of admitting; hence, both were decreased in size and an approximate normal maintained between them, so that the actual functional stenosis was reduced to a minimum—a condition further evidenced by the lack of hypertrophy of the right auricle; and these facts, also, are arguments of a lessened systemic circulation.

Assuming, then, an excessive pulmonary circulation, the mechanism of the functional compensation is rather easily imagined.

Beginning with the ventricular systole, we have both ventricular chambers filled with blood, the left containing the normal amount for the individual, as evidenced by the lack of either dilatation or hypertrophy of is walls. Systole occurs and the streams are forced in the usual directions, the lungs receiving a large influx —and we may recall here that the patient was "always more or less inclined to dyspnea"—while never, at any time, exhibiting any other sign or indication of cardiac or valvular defect, which

shortness of breath may be attributed to the large amount of blood which required aëration. Returning, the left auricle receives the inflow from the lungs, which, excessive in amount, necessitates a dilatation of that cavity, and this, it may be recalled, was found at autopsy; the right auricle, however, receives a comparatively small amount of blood, the relatively small incoming stream from the cavæ. This being in auricular diastole, when the auricles are relaxed, immediate admixture of the two streams occurs; but instead of the two amounts being equal, there is a comparatively small amount of venous blood thrown into a comparatively large amount of arterial blood returning from the lungs, which, therefore, diluted the venous blood to an extent sufficient to markedly reduce the element of contamination. Hence, when auricular systole occurs, the left ventricle, instead of receiving (to speak figuratively) a mixture of 50 per cent. venous and 50 per cent. arterial blood, receives a mixture of 80 per cent. arterial and 20 per cent. venous blood—a proportion theoretically containing sufficient oxygen to supply the needs of the tissues, when we remember that the systemic circulation is assumed to be decreased in amount. The dilatation of the right auricle is readily accounted for by the fact that part of the large amount of blood received into the left auricle—to which must be added that leaking in from the right auricle—is forced into the right auricle by the contraction of the left in the absence of the septum.

Such a supposition would also readily account for the dyspnea which would be consequent upon the large amount of blood in the pulmonary circulation, causing a rapid and increased gaseous interchange.

The hypoplasia of the aorta we are utterly at loss to explain the normal condition of its walls seems evidence in favor of the condition being congenital.

The mitral stenosis we believe to be partly congenital, in that the valve was probably never as large as it should have been, and partly due to the original infection from which the patient suffered a year before her death, and following which she eventually developed symptoms which led her physician to make a diagnosis of cardiac disease. The lesions of the tricuspid valve we also refer to the preceding endocarditis, both valvular lesions being chronic in type.

The entire case presents a problem at once puzzling and complex, which is not readily capable of satisfactory explanation, and it is to be regretted that, owing to the stipulation made when permission was given for the autopsy, the specimen could not be preserved for complete and minute examination, and, also, owing to the limited time in which the autopsy was made, that no photographs could be taken.

Had only some suspicion of the cardiac defect been aroused,

electrocardiagrams and tracings might have aided in shedding some light on the conditions of the circulation.

We regret that we were unable to search the literature for references to analogous conditions which may have been reported, or to make a careful search for references which might have been of service in the possible explanation of the case; the conditions as found, however, are sufficiently unusual and interesting to warrant some record, no matter how superficial or how unsatisfactory.

We would express our thanks to Dr. Alfred Stengel, in whose service the case occurred, for permission to report it; to Dr. Kenneth M. Lynch, who made the autopsy and was kind enough to go over it with the writer in detail; to Dr. E. R. Samuel, who copied the diagram accompanying the report; to Dr. Allen J. Smith, for facilities extended in the Laboratory of Pathology.

REVIEWS

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics, Materia Medica, and Diagnosis in the Jefferson Medical College; assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College. Vol. I, March, 1914. Pp. 406; 25 illustrations. Philadelphia and New York: Lea & Febiger.

THE first volume of *Progressive Medicine* for this year opens with an article on the surgery of the head and neck, by Charles H. Frazier. He takes up in great detail the pineal body, trigeminal neuralgia, and surgery of the auditory nerve. He also devotes considerable space to cancer of the oral cavity. The last part of his article deals with tuberculosis and carcinoma of the mammary gland.

In a 32-page article by George P. Müller, the surgery of the thorax, excluding diseases of the breast, is taken up. Intratracheal insufflation anesthesia, the surgery of the heart, the surgical treatment of tuberculosis, and carcinoma of the esophagus are the most important subjects dwelt upon by him.

Infectious diseases are reviewed by John Ruhräh, who as usual has written an instructive article. In his contribution of 127 pages all the important infectious diseases and many of the rarer ones are carefully discussed, and the most recent views regarding them are set forth.

An interesting contribution on diseases of children is furnished by Floyd M. Crandall. He devotes considerable space to the important subject of infant feeding.

In a short article of 55 pages, George B. Wood has furnished a thorough, careful, and up-to-date review of rhinology and laryngology.

An interesting article on otology has been written by Arthur B. Duel, who takes up the recent advances in this specialty in the course of a 46-page contribution.

This volume adequately maintains the high standard which is invariably found in this excellent work of reference. G. M. P.

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A Text-book of Pathology. For Students of Medicine. By J. George Adami, M.A., M.D., F.R.S., Strathcona Professor of Pathology, McGill University, and John McCrae, M.D., M.R.C.P. (Lond.), Lecturer in Pathology and Clinical Medicine, McGill University. Pp. 759; 304 engravings and 11 colored plates. Philadelphia and New York: Lea & Febiger.

In spite of the large number of works on pathology that are obtainable, there has existed for a long time a crying need for a thoroughly up-to-date text-book on pathology in English. The present volume fulfils all the requirements that are essential to a useful and adequate text-book, designed particularly for medical students and practitioners. By the exercise of extreme care and excellent judgment, the authors have accomplished the difficult task of condensing into a single volume of convenient size an unusually complete and thorough, yet clear and concise discussion of the entire subject of pathology. Their long experience as skilled teachers has evidently enabled them to appreciate the needs of the student, for throughout the book non-essentials are omitted, fundamental principles are dwelt on, and those phases of the subject that are of prime importance and which it is imperative for the student to grasp are emphasized and clearly explained.

In Part I the first chapter deals with the morphology, physiology, and chemistry of cells, together with certain other properties of cells and tissues, such as multiplication, adaptations, differentiation, and inheritance. In subsequent chapters the causes of disease and the various morbid and reactive processes, such as inflammations, infections, and immunity, etc., are taken up. The section concludes with chapters on progressive tissue changes as overgrowths, regeneration, metaplasia, etc.; and the tumors and regressive changes which include the degenerations and infiltrations, necrosis and death. The clearness with which certain complicated subjects are handled makes this section on general pathology noteworthy.

Part II deals with special and systemic pathology. In this section the disease processes peculiar to the various organs and systems of the body are discussed. All the chapters in this second part are well done, but the chapters on the cardiovascular system and the urinary system are of particular interest.

As a piece of book-making the volume leaves nothing to be desired, the beautifully clear type and many excellent illustrations add much to the usefulness of the book.

It is not too much to say that Adami and McCrae have written the best text-book on pathology that has yet appeared as a single volume in English. The warm welcome which has uniformly been accorded this work by pathologists, and especially teachers of pathology, was to be expected, and is amply justified by the unusual merit of the book. G. M. P.

A MANUAL OF SURGICAL TREATMENT. By Sir W. WATSON CHEYNE, Bart., C.B., D.Sc., LL.D., F.R.C.S., F.R.S., Hon. Surgeon in Ordinary to H. M. the King; Senior Surgeon to King's College Hospital; and F. F. BURGHARD, M.S. (Lond.), F.R.C.S., Surgeon in King's College Hospital and Consulting Surgeon to the Children's Hospital, Paddington Green. New edition, entirely revised and largely rewritten, with the assistance of T. P. LEGG, M.S. (Lond.), F.R.C.S., Surgeon to the Royal Free Hospital and Assistant Surgeon to King's College Hospital; and ARTHUR EDMUNDS, M.S. (Lond.), F.R.C.S., Surgeon to the Great Northern Central Hospital, Assistant Surgeon to King's College Hospital. In five volumes: Vol. V, pp. 619; 152 illustrations. Philadelphia and New York: Lea & Febiger, 1913.

THIS volume, which concludes the new edition of this useful work, discusses the surgical affections of the pancreas, liver, and spleen; surgery of the neck; surgery of the breast, thorax, and thoracic viscera; surgery of the genito-urinary organs (of the male); and concludes with an appendix, in which an attempt has been made to describe in the compass of less than ten pages "operations on the female genital organs, which may be found necessary in the course of an ordinary laparotomy." This latter phrase implies that in most cases the diagnosis is not made until after the surgeon has "taken off the lid." Such we are sure is not actually the case in King's College Hospital, or in any other hospital served by so able surgeons as the writers of these volumes; but it does seem strange for the authors to describe abdominal hysterectomy for myomata, removal of broad ligament cysts, and the "operation for extra-uterine fetation" as procedures which may unexpectedly become necessary after the abdomen has been opened for chronic appendicitis or some undiagnosed acute abdominal condition. The authors express regret that lack of space forbids them going "more fully into the various conditions of the female genital organs which require laparotomy," because they "are strongly of the opinion that the operation should only be performed by a surgeon who is prepared to deal with any abdominal condition that may be met with, and that no one should open the abdomen who is only able to treat some special organ." This sounds very well, and no doubt is the proper view to take; but it is one which can very easily be pushed too far. Thus one might forbid operations on any part of the female genital tract by those not qualified to treat any condition that may be met with in that tract; he might do the same for the male genito-urinary tract, and permit no one to perform a circumcision unless he were equally qualified to do a nephrectomy or at least a prostatectomy; he might forbid anyone to operate for a wen of the scalp, or to trephine in a case of depressed fracture of the skull, unless he were also competent to extirpate the Gasserian ganglion or remove a brain tumor. This clearly is

a *reductio ad absurdum;* but the principle holds good, and it is no more blameworthy for a "gynecologist" to feel a Hallerian diffidence about undertaking a partial gastrectomy or even a choledochotomy should he unexpectedly meet with a state of affairs rendering these operations proper, than it is for an "abdominal surgeon" to be overwilling to invade the pelvis when he has not sufficient skill to make in advance a reasonably correct diagnosis in the presence of an obscure condition in which the pelvic organs may be involved.

Affections of the male genital organs are discussed at a length of 167 pages, and 168 pages are devoted to the surgery of the bladder and kidneys. It certainly seems that these sections might have been curtailed with advantage if more room could thereby have been gained for the surgery of the female genitals, since in the average general surgeon's experience the latter occupies a much larger and more important place than genito-urinary surgery.

The other divisions of the book, dealing with abdominal and thoracic surgery, and affections of the neck, leave little to be desired. Perhaps a little more of the "newer surgery" of the thorax might have been included; a fuller description of the difficulties often encountered in choledochotomy in the absence of the gall-bladder would have been desirable; and it might have been well at least to mention that many surgeons now begin the operation for carcinoma of the breast by the axillary dissection, and that most of them deem it imperative to remove the pectoralis minor as well as *all* of the pectoralis major in every case.

On the whole, the volume can scarcely be said to equal those which have preceded it; but taken all together they form a most convenient and useful work of reference. A. P. C. A.

A Text-book of the Practice of Medicine. By James M. Anders, M.D., LL.D., Professor of Medicine and Clinical Medicine, Medico-Chirurgical College, Philadelphia. Eleventh edition, pp. 1335. Philadelphia and London: W. B. Saunders Company, 1913.

Doctor Anders' text-book needs no further recommendation than to say that this the eleventh edition is fully up to the standard of the previous ten editions that have appeared from time to time in the past seventeen years. One criticism might be made, that there is included in the text additions that have not as yet been carefully tested, so that some of them already have proved to be fallacious. Another change that it is hoped will be found in the next edition, is a revision of the sections upon lithemia and intestinal auto-intoxication. These are but minor points, however, that are truly obscured by the general excellence of the whole book. J. H. M., Jr.

ANATOMY, DESCRIPTIVE AND APPLIED. By HENRY GRAY, F.R.S.. Fellow of the Royal College of Surgeons; Lecturer on Anatomy at St. George's Hospital Medical School, London. A new American from the eighteenth English edition; thoroughly revised and reëdited, with the Basle Anatomical Nomenclature in English. By ROBERT HOWDEN, M.A., M.B., C.M., Professor of Anatomy in the University of Durham, England. Pp. 1407; 1126 illustrations. Philadelphia and New York: Lea & Febiger, 1913.

IT is scarcely necessary to advertise or review the successive editions of Gray's *Anatomy*. There never was such a book, and "none but itself can be its parallel." This edition, from the eighteenth English edition, has been edited by Howden, and is, we believe, the most satisfactory edition of Gray's *Anatomy* now on the market. The bulk of the volume has been reduced by about 200 pages, and this appears to have been accomplished by condensation rather than by omission. The histology of the elementary tissues and general embryology are discussed at a length of 160 pages at the beginning of the volume, rendering this portion of the work more useful for the student and handier for reference than when as in former editions these sections were scattered throughout the volume. The histology of more highly specialized tissues is considered along with the organs to which they are specially related.

The sections on surface anatomy have also been assembled, and are placed at the end of the volume, where this important subject may be studied without paging through the entire book.

Especially valuable, as in all editions of Gray, are the paragraphs on applied anatomy, appended to each section of the work. All of these are admirable in conciseness and lucidity, and most of the operations described truly represent modern surgery; but one is amazed at the barbarous method of panhysterectomy recommended at page 1254.

The Basle Anatomical Nomenclature is given in English, but whenever this necessitates a marked change in terminology the old terms, so long familiar, are also given in brackets. Especially in the nervous system are the advantages of this terminology apparent; in a former edition of Gray the task of ascertaining what the editor of the section on neurology was talking about was far too great for the average intellect. The editor is so careful, moreover, that he gives a complete Glossary of the Basle Anatomical Nomenclature at the end of the volume, so that any uncertainty as to meaning which may arise may be quickly dissipated.

Many new illustrations (about 200 in all) have been added, many of them replacing those in former editions, but a number of them are additional. Though the total number of illustrations has been decreased from 1149 in the edition of 1908 to 1126 in

the present edition, many of the figures in the former edition can well be spared: they were not worthy of Gray. These new illustrations, however, are of the highest type, many of them being in colors. Among the best of the latter are illustrations of the joints, of surface anatomy, of the abdominal organs, and of the lymphatics.

Constant use of the book serves to confirm the publishers' statement that "as a teaching instrument the new Gray's *Anatomy* embodies all that careful thought and unstinted expenditure can combine in a text-book." A. P. C. A.

A Text-book of Physiology. For Medical Students and Physicians. By William H. Howell, Ph.D., M.D., Professor of Physiology, Johns Hopkins University, Baltimore. Fifth edition. Pp. 1020; fully illustrated. Philadelphia and London: W. B. Saunders Company, 1913.

The first edition of this admirable book was so excellent in plan and execution that subsequent editions have brought about fewer changes than would be expected if the great strides in physiology alone were considered. Substantial physiology, the kind which will stand the test of time, was presented in a most lucid form. It is true that some material found its entrance which required further verification, but the author here was extremely careful in its discussion, emphasizing the shortcomings of the available material. As subsequent evidence accumulated the additions or subtraction which were necessary involved comparatively little space. Thus, the fundamental basis of the book was so excellent that new editions required comparatively few changes. The new discoveries have been weighed properly and conservatively by the author and not introduced unless well established and of value to the student and practitioner. Consequently, we are not surprised to find that the present edition has not exceeded the preceding in size, and that many pages remain absolutely unaltered. Nevertheless, as we page through the fifth edition and compare it with its predecessor we note that the author has a splendid command of the new unfoldings which have come to light in the last two years, the period which has elapsed between these two editions.

The greatest number of changes occur in the chapters on digestion and metabolism. The work of Hewey and Bensley on the origin of hydrochloric acid is given brief notice, and that of Stone and Bernheim which may throw some light upon the fatal effect of high intestinal obstruction in man. The text has received considerable recasting in the discussion of the fate of the absorbed products of digestion, particularly that of protein. In this connection the vitamines receive their just due. The recent work on the reductions and oxidations in the body are also referred to with perhaps sufficient emphasis.

The chapter on the internal secretions has also undergone important revision, the suprarenals are given more space in their consideration, the work of Cushing in connection with the pituitary body is referred to, as are also the interesting observations of Steinach upon the internal secretions of the testicles. The chapters on reproduction and secretion also show evidence of careful attention although the changes are comparatively few.

The edition will undoubtedly find the continued favor which the preceding editions have had. E. L.

EARLY PULMONARY TUBERCULOSIS: DIAGNOSIS, PROGNOSIS, AND TREATMENT. By JOHN B. HAWES, 2d, M.D., Assistant Visiting Physician, Director Tuberculin Department, Massachusetts General Hospital; Secretary, Board of Trustees Massachusetts Hospitals for Consumptives. With Preface by RICHARD C. CABOT, M.D., Assistant Professor of Medicine, Harvard University. Pp. 114; 45 illustrations. New York: William Wood & Co., 1913.

THE salient features of early pulmonary tuberculosis have been much dwelt upon and may all be found somewhere in the vast literature of tuberculosis, but nowhere can they be found so conveniently grouped or stated with such conciseness and authority as in this small book. Peculiarly well fitted for the task by reason of careful training and large experience, Hawes has handled this vital subject with rare judgment, and has emphasized its importance with effectiveness the more telling because of the terse, epigrammatic style in which he writes. Such a sentence as, "If the stethoscope were used less and the thermometer more, fewer mistakes would be made" well illustrates how he drives home an important point.

The book deals solely with the problem of *early* tuberculosis, and particularly its diagnosis. The various facts that should be especially considered in the history of such patients are first taken up. Hawes then discusses the signs and symptoms that should be noted in these cases. His sixth chapter, on the adventitious signs in the chest not due to tuberculosis, but often mistaken for evidence of pulmonary disease, and the tenth chapter on conditions which may simulate tuberculosis are worthy of note. In addition, he discusses the value of tuberculin and the *x*-rays in the early diagnosis of tuberculosis, as well as bronchial gland tuberculosis in children, the prognosis and course of early tuberculosis, and its treatment. The book concludes with five appendices in which are given the histories of illustrative cases, a reliable method for staining tubercle bacilli in sputum, photographs and *x*-ray pictures of characteristic types of chests, data in reference to the Massachusetts tuberculosis

sanatoria, and finally valuable directions for living and sleeping in the open air.

The book is obviously the work of one so thoroughly master of all the details of the subject, as well as its literature, that he is capable of stating with refreshing frankness and assurance the most reliable modern views in regard to tuberculosis.

The book was written for a definite purpose, namely, to help the general practitioner, and it should well fulfil its mission. No one who reads it thoughtfully can fail to receive from it a clearer conception of the value and importance of the early diagnosis of pulmonary tuberculosis. G. M. P.

STAMMERING AND COGNATE DEFECTS OF SPEECH. By C. S. BLUEMEL. 2 Vols. Pp. 741. New York: G. E. Stechert & Co., 1913.

THIS work should have been called "A Theory of the Basic Cause of Stammering," as clinical cases supporting the author's views are not cited and the method of cure is a proposition without verification, sketched in its broadest and most general aspect.

The work is published in two volumes, the first volume is an orderly presentation of subjects germane to stammering—psychological considerations, brain localization, aphasia, the mental condition of the stammerer, and the different forms of stammering, with a short final chapter on the author's principles of treatment. It must be said that this is done so well, and with such eveidence of study shown by interesting quotations from Bastian, Galton, James and others, that it is worth reading.

The author's contention is that "pure stammering" is altogether mental and is due to weak auditory memory—a transient auditory amnesia. Other possible elements in the cause (fear, bewilderment, inhibition of the will from auto-suggestion, perversion of the verbal imagery) are secondary complications.

The method of cure advocated, and to the author the only scientific and effectual one, is the supplementing of the weak inert auditory imagery by visual and kinesthetic imagery. In other words, the stammerer memorizes by observation and practice the proper muscular movements to produce the desired sounds. He then produces the desired sound, or at least starts it, by pure muscular memory. This method, as we all know, is the one used in teaching the congenital deaf to speak.

The second volume discusses the different principles on which various treatments for stammering have been based—respiratory exercises, vocalization and vowel production, articulatory modes of enunciation, mechanical appliances, and psychological methods.

Altogether the book is well worth reading and a very valuable contribution to the subject. W. S. C.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Etiology of Variola and Vaccine.—E. PASCHEN (*Deutsch. med. Woch.*, 1913, xxxix, 2132) presents the evidence thus far collected which tends to show that the bodies which he has been studying for a number of years are in reality the causative agent of variola and vaccine. The bodies are very small, round, sharply defined, coccus-like objects, which divide directly. On many of these bodies one can see a very delicate, filamentous process. Frequently the bodies are found in pairs, which are united by a filament; this appearance is even more striking with dark field illumination. The two bodies seem to dance about, approaching and receding from one another. As von Prowacek has shown, this is Brownian movement. Often there is a halo surrounding the bodies. It has been demonstrated that they pass through the Berkefeld filter. They are stained with difficulty, but satisfactory preparations may be obtained by first treating with Loeffler's mordant and then staining with carbol-fuchsin, carbol-gentian violet or carbol-methyl violet. The intensity of the staining is influenced by the apparent size of the bodies and also by the thickness of the surrounding layer of serum. There is considerable variation in size, but the largest of the bodies are less than 0.5 micron in diameter. With Giemsa's mixture, they are stained faint blue and are easily decolorized. The bodies are chiefly intracellular; after inoculation they enter the epithelial cells and multiply rapidly in them. They are very resistant; they are not dissolved by 2 per cent. potassium hydrate, 2 per cent. acetic acid, chloroform, alcohol, ether, distilled water, or physiological salt solution. They are agglutinated by specific immune serum. In the lesions of other skin affections, the bodies found in variola and varicella have not been discovered.

Experimental Hyperglycemia in Man through Intravenous Injections of Sugar.—S. J. THANNHAUSER and H. PFITZER (*Münch. med. Woch.*, 1913, lx, 2155) have attempted to shed new light on sugar metabolism by studying the effects of intravenous injections of glucose in health and disease. For the determination of glucose in the blood they have employed Bang's method, which is accurate with minute quantities of blood. They have determined the blood glucose before the injection, when half of it had been administered, and at the completion of the injection. Determinations were also made every five minutes for the first quarter of an hour after the injection, then after one, four, and twelve hours had elapsed. Thannhauser and Pfitzer employed a 7 per cent. solution of glucose which had been carefully pasteurized; they injected 500 c.c. of this intravenously, equivalent to 35 gm. glucose. The normal individual excretes a trace of sugar in the urine after the intravenous injection of 20 gm. glucose. As in alimentary or subcutaneous administration of glucose, a marked increase in the amount administered produces only a slight increase in the sugar in the urine (0.1 gm. to 0.5 gm.). Thannhauser and Pfitzer find that the quantity of blood sugar reaches the normal level in one-quarter of an hour after the injection. Here hyperglycemia leads to glycosuria. In patients suffering with disease of the liver (lues, metastatic cancer, cirrhosis), the conditions were found to be quite different. The glucose excreted in the urine (0.5 to 3 gm.) is only slightly greater than in the normal, but the hyperglycemia persists for hours without glycosuria. In chronic nephritis, in which blood glucose is usually in excess of the normal, there is a sharp rise in the blood sugar curve with a return to the previous level within one quarter of an hour and only a slight glycosuria (0.2 to 0.44 gm.). In severe diabetes all of the injected sugar is excreted in the urine; the increased percentage of blood-sugar caused by the injection is maintained for several hours. The carbohydrate depots are apparently unable to warehouse the excess. In mild diabetes the findings are similar to those in normal individuals.

The Benzol Therapy of Leukemia.—E. MÜHLMANN (*Deutsch. med. Woch.*, 1913, xxxix, 2083) utters a word of warning regarding the use of benzol in the treatment of leukemia. He reports the findings at autopsy in a patient with lymphatic leukemia treated with benzol, the amount given varying from 0.25 to 3 gm. daily, with intermissions of a few days occasionally. At autopsy there were found liver necroses affecting the central parts of the lobules. Since Neumann has reported similar findings in the liver in a patient with myeloid leukemia treated with benzol and as hepatic injury is frequent in animals which have been given benzol, Mühlmann thinks it very likely that the hepatic lesions in his patient and in Neumann's case are attributable to the benzol. He urges caution in the employment of this drug.

Thymin in the Treatment of Exophthalmic Goitre.—R. HIRSCH (*Deutsch. med. Woch.*, 1913, xxxix, 2141) finds, as do most observers, that Basedow's disease is very rare in childhood. Furthermore, she observes, children are very tolerant of preparations of the thyroid gland. These considerations led her to try the administration of thymus gland to patients suffering with hyperthyroidism. Thymin,

manufactured by Poehl, is the preparation used. Two tablets of 0.5 gm. have been given daily. Hirsch has tried this treatment in 12 cases and says the results have been quite encouraging. Details of cases are reserved for a later contribution. She finds that thymin has an elective action on cardiopathies of thyreotoxic origin. As she noted that the sleep of patients with hyperthyroidism is much improved by administration of thymin, she has employed it as a hypnotic. Hirsch administered it for this purpose first to two patients with diabetes insipidus (Wassermann reaction negative in each case). The sleep of each patient had been disturbed by the necessity of drinking water and urinating frequently. One tablet was given in the morning and two at night. After instituting this treatment, both patients promptly began to sleep through the entire night and other symptoms were also improved. Two tablets at night have produced restful sleep in neurasthenics.

Observations on the Blood Sera of Gouty Individuals.—E. EHRMANN and H. WOLFF (*Münch. med. Woch.*, 1913, lx, 2115) have made observations on the uric acid content of the blood of normal and gouty subjects. They summarize their findings as follows: (1) On a purin-free diet the blood serum of normal individuals contains sufficient uric acid to estimate quantitatively. (2) Cases of typical gout on a purin-free diet present the same (or lower) values for uric acid as the normal sera. (3) Therefore, determination of the uric acid in the blood serum is of no value in the diagnosis of atypical gout. (4) A few hours after the administration of atophan the uric acid of the blood is unchanged; in one instance it became so low that it could not be determined. In an acute attack of gout, during the administration of atophan, the uric acid was much lower than it was a few days later. (5) Uric acid is practically always more abundant in the blood serum than the purin bases, contrary to Wiechowski's findings with whole blood. (6) The hydrogen ion concentration is much higher in gout than normal and also higher than in diabetic coma. This indicates a decreased alkalinity of the blood in gout. (7) In some cases of gout a lipemic appearance of the blood was noted.

Further Studies on Experimental Syphilis.—P. UHLENHUTH and R. MULZER (*Berlin. klin. Woch.*, 1913, xlix, 2031) report further studies on experimental syphilis which throw additional light on the pathology and therapy of the disease. Uhlenhuth and Mulzer summarize their results as follows: (1) In latent syphilis (positive Wassermann without clinical evidence of the disease) they have not yet succeeded in demonstrating the infectivity of the blood through inoculation of a rabbit's testicle. (2) Animal inoculation does not furnish conclusive evidence of the efficacy of therapy. (3) Positive inoculation experiments with the blood of patients showing the signs of tertiary syphilis have been obtained, though this seems not to be the rule. (4) The inoculation of the blood of patients exhibiting signs of a late hereditary syphilis (gummas, keratitis, positive Wassermann) has invariably given negative results. (5) A number of inoculations of the saliva and the urine of patients suffering with a recent lues have thus far given negative results. (6) In a recent case Uhlenhuth and Mulzer have again been able to demonstrate the infectivity of the semen.

They have also succeeded again in showing that the milk of a mother free from symptoms, who had given birth eight days previously to a syphilitic infant, was infectious to the rabbit. (7) The blood as well as bits of tissue from the eruptions of a patient suffering with "malignant" lues, when inoculated into rabbits, almost invariably produced a syphiloma of the testis rich in spirochetes. (8) The spinal fluid of 2 recent cases was shown to be infectious. (9) Blood and spinal fluid of tabetics and paralytics have always given negative results on inoculation. (10) In one case they succeeded in producing a typical lesion in the rabbit's testicle by inoculation of a suspension of the brain of a paralytic. (11) Liver and spleen of syphilitic rabbits seem to be more infectious than the other internal organs. (12) Dilutions of 1 to 1000 (2 c.c.) of the usual syphilitic testicle emulsion may give positive results on inoculation.

Experimental Syphilis of the Nervous System.—A. JAKOB and W. WEYGANDT (*Münch. med. Woch.*, 1913, lx, 2037) report observations on the histology of the nervous system of rabbits infected with syphilis. They find that experimental syphilis, like the human infection, leads to a wide dissemination of the spirochetes in the body. Both the central and the peripheral nervous systems are affected relatively early; frequently there is meningeal involvement. In all the experimental animals severe inflammation and infiltration are seen; these changes originate in the mesodermal coverings or in the bloodvessels of the entire nervous system. By extension the nervous parenchyma becomes involved. The cells concerned in the infiltrative process are chiefly lymphocytes, plasma cells, and polyblasts. Of particular interest are the localized processes. These may consist of granulation tissue with large numbers of plasma cells, both in the peripheral and central nervous systems, with tumor formation, or there may be a localized collection of plasma cells in the neighborhood of a markedly infiltrated vessel which has led to severe degenerative and proliferative changes in the contiguous nervous tissue.

SURGERY

UNDER THE CHARGE OF

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The Removal of Ascites.—KUMARIS (*Zentralbl. f. Chir.*, 1913, xl 1916) removes as much as possible of the parietal peritoneum in order to produce abundant adhesions between the viscera and abdominal

wall. The absorptive capacity of the peritoneum removed has very probably been diminished, and after the operation the direct escape of the fluid is more easy. The eventual, extensive adhesions between the viscera and the extraperitoneal tissues gives rise to an abundant collateral circulation. This is supplied particularly by the omentum, but all the other organs contribute. Kumaris reports the following case, illustrating the application of the method: A woman, aged fifty years, suffered from malarial ascites, for which it was necessary to withdraw the fluid by puncture every fifteen days. The circumference of the trunk at the umbilicus was 110 cm., and there was edema of the ankles. Forty-eight hours after removal of the fluid by puncture a 19-cm. incision was made in the median line above and below the umbilicus. The liver and spleen were contracted and rough. On each side of the incision a strip of the silver white and thickened peritoneum, 25 cm. by 25 cm., was removed. The omentum was fixed to this surface by two sutures. Layer sutures of the abdominal wound were employed. Forty-eight hours after operation the limbs showed a "dry skin," and the swelling had disappeared. This did not follow the previous punctures. Eight days after the operation the circumference of the trunk was 85 cm., and fifteen days afterward 80 cm., while the general condition was good. Unfortunately on the following day there developed a very severe erysipelas of the face and the patient died twenty-two days after operation. The abdomen was then soft and contained only a small quantity of fluid and had a circumference of 80 cm.

The Diagnosis of Dislocation and Fracture of the Semilunar Cartilages.—AARAU (*Zentralbl. f. Chir.*, 1913, xl, 1852) says that sometimes the symptoms are completely negative, so that the operative indication rests upon an exact history. In such cases Aarau has found a systematic auscultation of the knee-joint of advantage. There is no sound characteristic of an injured meniscus. In some clinically evident cases, at the moment when the injured cartilage is torn from its place, a rather loud cracking sound is heard. It is in such cases that the meniscus is torn from its attachment in a large extent and sometimes is completely separated. It is much more difficult to diagnose those cases in which the meniscus is only partly torn away and which give only few clinical symptoms. In these a comparative auscultation of both knees will bring out a difference in sound. On the unaffected side little or no sound will be heard. Even on strongly forced movements only a slight cracking sound will be detected here and there. On the affected side, whether the internal or external meniscus be involved, by slow movements, a rubbing sound, and by extensive and forced movements, a cracking sound is perceptible. Sometimes a very loud sound is heard. It is louder on flexion than extension. In 6 out of 7 cases operation established the diagnosis thus made. Auscultation is best made with both ears by a stethoscope, the bell of which is provided with a rubber ring to overcome the effect of the uneven surfaces about the knee. Auscultation should be tried in the standing position with marked flexion of the knee, as well as in the recumbent position. The joint-space on both sides of each joint should be ausculted and the differences noted.

Sun-treatment of Tuberculosis of the Foot.—LEUBA (*Deutsch. Zeit. f. Chir.*, 1913, cxxv, 413) gives a *resume* of the results of the exposure of tuberculous feet to the sun, in Rollier's clinic. The patient is first confined to bed and for a time (three to fifteen days) is constantly exposed to the sun all morning, different portions successively until the whole body has been covered. By gradually increasing the extent of the exposure finally the whole body is exposed at one time. In a similar manner the time of exposure is gradually increased until finally the patient can remain exposed for four hours at a time, without disturbances of the skin, the nerves, or the heart. The treatment of the foot is as follows: The affected foot is placed on an even surface, so inclined that the foot is higher than the pelvis. The tendency to the equinus position is combated by the use of a removable plaster splint which permits mobilization. The sinuses are exposed to the sun without any dressing, and to the free air in the absence of sunshine. At night they are merely covered with compresses. No injections nor operations are employed. When healing is obtained, as demonstrated by the *x*-rays, the patient returns to his home and for at least a year wears an apparatus by means of which the support is taken at the knee and the patient places no weight on the recently healed foot. The combination of the fresh air and sunbath produces a return of strength in the whole organism, which is essential for the cure of surgical tuberculosis. These patients with their bronze-colored skin, which remains uncovered for the greater part of the day, are resistant to changes in the temperature. The fever usually falls rapidly, the appetite increases, digestion regulates itself, and the respiratory capacity is improved. The hemoglobin index is frequently greater than normal. Locally the pain disappears and the swelling and contractures are much relieved. Fistulæ and granulation tissue gradually diminish and sequestræ are separated. Abscesses may be absorbed but it is best to remove the pus by punctures. Tuberculous joint affections exposed to the sun heal without atrophy and often without ankylosis.

Acute Hemorrhagic Pancreatitis.—RUNGART (*Deutsch. Zeitsch. f. Chir.*, 1913, cxxv, 530) studied 7 cases from Tilmann's clinic. In all of the cases there was the sudden development of the severe symptom-complex, the malignant and stormy course of the whole process and the characteristic relation between the pulse and temperature. Most of the cases began with a severe pain in the upper abdomen and a simultaneous cessation of intestinal activity. From a previous excellent general condition, they pass rapidly, in a few hours, into a severe condition of collapse with a striking incongruence between the temperature and pulse. The temperature generally remained about normal while the pulse mounted to 120 and higher and was small and soft. All but one of his cases died. All authors agree now on the necessity for early operation in order to drain the extravasated pancreatic secretion, and the discharge from the necrotic tissue. The best method of drainage varies with the type of case. Those in which the symptoms present, chiefly, anteriorly, should be drained by the transperitoneal route with splitting of the capsule, sponging away the exudate and applying a tampon over the gland. In the dorsal form

drainage should be provided from the flank or back by a retroperitoneal tampon. The main point is to decide upon operation in every case, even in those in which the presence of pancreatitis is only suspected. In the great majority of cases an exact diagnosis cannot be made until the best time for operating has passed. It is in such cases that exploratory laparotomy has its best justification. A troublesome fistula frequently follows operation. Wohlgemuth has shown that a diet with the carbohydrates decreased or absent and with the avoidance of acids, will cause a considerable decrease of the pancreatic secretion which makes the fistula troublesome.

Deaths from Anesthesia and Lessons to be Drawn from Them.—Cotton (*Annals of Surgery*, 1913, lviii, 934) says that the fact that he or any surgeon can report 10 deaths and 3 close approaches to death from anesthesia personally observed in the course of two or three years, is of itself evidence that the old delusion of the safety of anesthesia can no longer be maintained. It has been maintained in the past, charging off to shock, heart failure, intercurrent pneumonia, alcoholism, etc., the great majority of cases that we ought not honestly regard as due to anything but anesthesia. Perhaps the propriety of classifying some of his list of cases as anesthetic deaths may be brought into question, but if they had not been anesthetized the trouble would not have occurred. We should have none but really skilled anesthetists. This is not yet possible, but we must keep hammering at the kind of anesthetists we have. One of his deaths was probably from acid intoxication, and in another failure to recognize and treat acidosis would, he believes, have lost the case. Often, no doubt, it is not important, if present, but it is well to bear in mind, and in case of doubt, sodic bicarbonate and early feeding by mouth or rectum is harmless and may change the issue entirely. Cotton bars absolutely any chloroform mixture as a preliminary. At best it calls for very expert handling, and he sees in practice few cases requiring its use Intratracheal anesthesia is for the man who knows how. Cotton's preference is for the gas-oxygen-ether combination.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Leukemia with Benzol.—Barker and Gibbes (*Johns Hopkins Hosp. Bull.*, 1913, xxiv, 363) describe briefly the results of benzol therapy in cases of leukemia and allied blood diseases which have been reported by various observers. They note a total of 18 cases from the literature, of which number 13 were cases of

splenomyelogenous leukemia and 2 were lymphatic leukemia. Barker and Gibbes add a case of splenomyelogenous leukemia that responded very favorably to benzol therapy. The course of benzol administration extended over approximately eleven weeks, during which period the total number of white blood cells returned to normal, the red blood cells increased from 3,600,000 to 5,000,000, with a corresponding increase in the hemoglobin content from 65 per cent. to 82 per cent. While their patient progressed in a satisfactory manner with benzol alone, they feel that the possible value of other accessory measures, such as *x*-rays, arsenic, thorium-X, and radium, in the therapy of leukemia should be kept in mind. Pappenheim's criticism of the benzol treatment, based upon a theoretical consideration of Selling's work and an attempt to apply some experimental studies has been replied to by von Korany. The latter author believes that the toxic manifestations in rabbits produced by relatively immense doses of benzol do not imply that similar effects follow upon the use of the drug as it is now therapeutically employed in leukemia. The ultimate place of benzol in the treatment of leukemia, polycythemia, and Hodgkin's disease can be determined only through further studies which include careful clinical observations. Barker and Gibbes emphasize the facts, first, that benzol does possess dangerous toxic properties; second, that its clinical effects are not yet clearly understood, and, third, that the greatest care should be exercised in its administration. A studious regard for the dosage as thus far determined, a watchfulness for the manifestations of poisoning that are well defined and easily detected, and a willingness to employ other measures in conjunction with this drug are means that will serve to give the new treatment a fair trial and prevent its falling into an undeserved disrepute. No patient should be treated by benzol unless he can be kept under continuous close observation; for the present, therefore, it may be well to restrict its use to the treatment of patients in hospitals.

The Action of Nitrites and Drugs of the Digitalis Group on the Isolated Coronary Artery.—Voegtlin and Macht (*Jour. of Pharm. and Exp. Therap.*, 1913, v, 77) relate their observations as to the effect of certain drugs upon the isolated coronary artery with particular reference to constrictor or dilator action of the drugs studied. They found that digitonin and digalin produce relaxation, while digitoxin, digitatin, and bufagin cause a constriction of the coronary arteries. Digitonin is probably responsible for the dilatation produced by digalen and the infusion of digitalis. All the nitrites were found to produce prompt relaxation. It was also found that the nitrites and digitalis-like bodies, can antagonize each other in their action. Voegtlin and Macht believe that the action of these drugs is similar on the intact mammalian heart and, therefore, whenever coronary spasm is to be avoided or guarded against, it would be advisable to employ the digitonin-containing preparations, or to simultaneously administer the nitrites. Furthermore, if angina pectoris is due to spasm of the coronary vessels, they believe their results explain the favorable action of the nitrites in coronary angina.

Vaccination against Varicella.—KLING (*Berlin. klin. Woch.*, 1913, l, 2083) vaccinated children with material derived from the pustules of children with varicella in an institution where there was exposure to the disease in an epidemic form. There was a positive response to the vaccinations in 58 cases where this procedure was applied. In the portion of the institution chiefly affected by the epidemic there were 95 children. Only 1 out of 31 vaccinated children developed the disease, while over two-thirds (44 out of 64) of those not vaccinated had typical varicella. The technique of the procedure is very similar to that of vaccination for smallpox. On the eighth day after the inoculation, one or usually several red papules develop that become vesicular within twenty-four hours. The vesicles are surrounded by a reddened area that increases in extent for two or three days. On the third or fourth day the vesicles dry up and in two and a half weeks the scab drops off. The general assumption that varicella is harmless and amounts to no more than a contagious skin disease is, according to Kling, very often false, and especially false in institutions where it may develop into a malignant form. Erysipelas and general septicemia may originate from secondary infection of the pustules, while pneumonia, nephritis, extensive gangrene of the skin are complications that are not rare in institutional cases.

The Effects of Emetine on Abscess of the Liver.—SPITTEL (*British Med. Jour.*, 1913, 2756, 1058) reports a case of probable amebic abscess of the liver treated by a combination of subcutaneous injections of emetine hydrochloride and surgery. This patient died, not from the liver abscess, but from too early removal of drainage tubes and subsequent infection of the peritoneal cavity. The noteworthy facts of this case were that the cavity in the liver, which at the time of operation contained one and a half pints of pus, was found nine days later to have a capacity for only four ounces, while a very rapid advance of fibrosis was proceeding throughout the abscess wall. Several separate foci of pus had been rendered inert and showed microscopically the beginning of fibrosis. Spittel believes that mere evacuation of pus and local treatment could not account for this result even if they did for the former. Spittel notes that Rogers has recorded a case in which encystment of a small liver abscess occurred under emetine. Spittel says that in future he will give preference to Roger's method of dealing with liver abscesses—namely, to aspirate them, inject emetine hydrochloride (1 grain to 1 ounce of water), before withdrawing the cannula, sealing the puncture with collodion, and repeating the procedure on a future occasion if required.

The Therapeutic Use of Camphor.—LEO (*Münch. med. Woch.*, 1913, lx, 2397), experimentally was able to protect mice against pneumococcus infections by subcutaneous injections of saturated solutions of camphor in water. He believes that camphor is able to kill pneumococci in the blood besides acting as a respiratory and cardiac stimulant. Leo gave the camphor solution in doses of 5 c.c. per kilogram of body weight in his animal experiments, but as this dosage produced muscular twitching he advises smaller proportional doses for its use in human beings. For this purpose he recommends a satu-

rated solution of camphor in Ringer's fluid, giving from 150 to 200 c.c. to patients having an average weight of 60 kilos. A saturated solution of camphor in Ringer's solution is equivalent to 0.142 gm. camphor per 100 c.c., and therefore these doses correspond to from 0.21 to 0.28 gm. of camphor. He quotes Lenzmann who has given 75 c.c., corresponding to 0.1 gm. camphor intravenously. No bad effects such as pain, infiltration, or thrombosis have been observed with the intravenous use. He constantly found an increase of blood pressure equivalent to 20 to 30 mg. of mercury as a result of these intravenous injections of camphor solutions. Leo says that Weintrand has also used intravenous injections of a 0.1 per cent. camphor solution, giving from 250 to 350 c.c. with no untoward local or general effects. He advocates the use of such a solution in place of the usual infusion of normal saline.

The Etiology and Vaccine Treatment of Hodgkin's Disease.—Billings and Rosenow (*Jour. Amer. Med. Assoc.*, 1913, lxi, 2122) confirm the findings of Bunting and Yates and Negri and Mieremet, who described a bacillus that they cultivated successfully from the lymph nodes in Hodgkin's disease. Billings and Rosenow were able to isolate such a bacillus from the lymph nodes in 12 cases of Hodgkin's disease. They treated these cases with autogenous vaccine except in one patient, who received the vaccine prepared from other patients. The vaccine was first given in the dose of from 5,000,000 to 10,000,000 and gradually increased to a maximum of 100,000,000. The vaccine was given subcutaneously and repeated every five to seven days. They have not used it intravenously, but have considered that method of application in obstinate and extreme conditions. In febrile patients the second or third dose has been associated with a reaction consisting of a rise in temperature (in one patient to 107° F.), rapid pulse, and general weakness and discomfort. In non-febrile patients only slight general reaction may occur with a rise of one or two degrees of temperature, slight general muscular aching and debility. In addition to the vaccine treatment they used Röntgen treatment in the majority of the cases treated. Billings and Rosenow state that in 6 of the hospital patients there was a uniform and relatively rapid decrease in the size of the lymph nodes, one of these without Röntgen treatment. One patient treated out of the hospital with the vaccines alone, with very large lymph nodes, markedly enlarged spleen and febrile, had a violent general reaction with the third dose, then became afebrile, and the swellings of the lymph nodes and splenomegaly rapidly diminished. Reports from physicians on two of this series show favorable progress with gradual diminution of the lymph nodes and general improvement. Two of the series died; one with marked enlargement of the mediastinal lymph nodes died soon after the third vaccination and the other, also with involvement of the mediastinal lymph nodes died from the result of mediastinal pressure after only one autogenous vaccination. One patient is apparently cured. There are no palpably enlarged lymph nodes; the formerly much enlarged spleen is no longer palpable; the blood picture is normal; his weight and strength are normal. Billings and Rosenow present this communication as a preliminary note with the hope that the clinical study may be carried on by others.

PEDIATRICS

UNDER THE CHARGE OF

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A Case of Rabies.—ALFRED HAND, JR. (*Archives of Pediatrics*, 1914, xxxi, 9) reports a case of rabies in a boy, aged nine years. The boy was severely bitten in the face by a dog. Pure carbolic acid, followed by alcohol was applied and the wounds dressed with gauze wet with a 1 to 1000 solution of bichloride. The next day the wounds were unusually inflamed and the boy complained of soreness of the jaws and difficulty in swallowing. The parents refusing the Pasteur treatment, the boy was not seen again until he was admitted six weeks later with headache, pain in the throat, and convulsions, during which, however, he did not lose consciousness. The boy developed a continuous activity, lying down, sitting up, and jumping from side to side. The face was flushed a light red and the pupils were widely dilated. There was spasm of the pharynx, and the saliva could not be swallowed but was spat out at intervals of a few seconds. The saliva consisted of small, sticky pellets floating in a watery secretion, which filled a pus-basin in a few minutes. Hypodermics of morphine had no effect on the spasm, but spraying the nasopharynx with a cocaine solution gave immediate relief. The boy took water into his mouth but was unable to swallow it. The body temperature was 106° F., but it was impossible to apply sponge baths owing to the excitement they produced. Later the paroxysms became less acute and there was perspiration, while the pupils again reacted to light, but the boy failed to respond to questions asked, as before. The parents removed the boy to his home, where he died fifteen minutes after his arrival. The boy's brain, examined by the State Livestock Sanitary Board, showed one ganglion cell containing three Negri bodies. One of the rabbits inoculated subdurally with the tissue died subsequently, and microscopic examination of the hippocampus revealed Negri bodies in large numbers. The diagnosis of rabies was made conclusively.

Edema in Infants.—HENRY DWIGHT CHAPIN (*Archiv f. Pediatrics*, 1914, xxxi, 5) reports a series of cases in which the symptoms were studied in their relation to edema. He recalls the fact that any marked bodily disturbance in infants is apt to show abnormalities in urinary findings. Thus the greater majority of mild and severe gastro-intestinal diseases along with most pulmonary diseases show small amounts of albumin in the urine, which, however, does not predicate the presence of actual renal disease. Therefore edema in infants cannot be considered as due to nephritis, because small amounts of albumin are found in the urine. Dwight observed and studied a series of 21 cases varying in age from sixteen days to three years. Among the diseased conditions present were malnutrition, 12; bronchopneumonia, 2; pericardial effusion, 1; otitis media, 2; cerebrospinal meningitis, 1;

and 2 were in apparent good health. The edema was general in 4 cases, and in the others was limited to the hands or arms, legs or feet, face or abdomen. The blood examinations showed no pernicious or profound anemia. Albumin was present as a faint trace in 9 out of 19 cases, and a heavy trace in 1 case. It was absent in 9 cases, and sugar was absent in all cases. Seven specimens showed occasional granular or hyaline casts. The duration of the edema varied from three to twenty-one days. There were 7 deaths: From malnutrition, 3; bronchopneumonia, 2; meningitis, 1; and pericarditis, 1. Dwight makes a rough classification of the kind of cases that are apt to show edema. First, difficult digestion and mal-assimilation through toxins inducing vasomotor paralysis, or conditions analogous to the urticarias. Second, in exhaustive conditions, prematurity, marasmus, etc. Third, constitutional diseases as syphilis, tuberculosis, erysipelas, etc. Fourth, angioneuroses of vasomotor origin, 2 of which class occurred in the above series.

Position of the Stomach in Children.—James Warren Sever (*Archiv f. Pediatrics*, 1914, xxxi, 38) reports his observations on the position of the stomach in children. These observations were made on a large number of children by means of the bismuth meal and the *x*-rays. A great diversity of opinion has existed among medical men as to the lower border of the stomach in health. From a great number of opinions the average would be at or just above the level of the umbilicus. It is a commonly stated fact that about one person in five is born with a congenitally defective support of the colon and stomach. Sever shows that in children, at least in 90 cases, the position of the stomach is normally much lower than has been suspected. Sever's method included plates taken after a bismuth meal with the child in the usual erect posture, using the crests of the ilia as a landmark instead of the umbilicus. The averages by age, height, and weight, of the cases were well up to or above Holt's averages for children of similar ages. General conditions and body weight were found to have very little to do with the position of the stomach. No relation could be established in regard to the shape or capacity of the thorax with the degree of ptosis present. A study of the *x*-ray plates of 83 children, taking the crests of the ilia as landmarks, showed the lower border of the stomach opposite the fourth lumbar vertebra in 25 cases; 9 showed it at the level of the crests, and in 49 cases the lower border was well below the crests, often in the pelvis, as much as 3 or 4 inches below the level of the crests. From this uniformly low position of the stomach in so many cases Sever concludes that the position is about normal for children. Few stomachs presented the so-called normal cow's-horn shape, the most persistent type being that of the sink-drain variety. But one of these children had symptoms referable to its digestive tract and this was due to a dilated colon. To find a stomach low in a child does not necessarily mean that there is a pathological ptosis.

OBSTETRICS

UNDER THE CHARGE OF

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Puerperal Pyemia.—WARNEKROS (*Archiv f. Gynäkologie*, 1912, Band xcvii, Heft 1), reports three interesting cases of puerperal pyemia in which operation proved unavailing, and in which interesting observations upon the nature of the disease were made. He believes that by studying the temperature curve of the patient without other data, that the occurrence of blood infection can be recognized and a fairly good idea obtained as to the severity of the infection and its anatomical spread. When a patient has had fever for some time and a chill occurs, repeated on the following day, and between the chills a very marked remission of temperature, either to or below the normal, one can diagnosticate local endometritis as the primary cause of the fever, and thrombophlebitis as the cause of the chills, with the entrance of masses of bacteria into the blood. When a patient has had atypical fever for some time, and the fever becomes high and continuous without chills, a direct invasion of bacteria into the uterine veins, either at the placental site or through wounds in the uterine mucosa, may be diagnosticated. Bacteriological examination is useful in controlling and correcting clinical data. So long as the endometritis is localized, the blood will be found sterile, and if chills occur, with continuous high fever, bacteria will be found in the blood. In pyemia with thrombophlebitis, bacteria are present in the blood at the beginning or during the chill itself; while in severe puerperal septicemia they are found continuously in the blood. From these observations one may gain indications for treatment. In thrombophlebitis, the blood during the interval between the chills is at least comparatively free from bacteria. This, then, is the favorable time for operation, as the infection is then localized. When bacteria are constantly present in the blood, ligation of the thrombosed pelvic veins may still be of some use in limiting the bacteria which enter the circulation. In one of his cases after ligature of the veins the bacteria disappeared from the blood. In operating upon thrombosed pelvic veins, he believes that the common iliac should be selected. If the thrombosis has extended still higher, the vena cava may be tied. The circulation will practically be restored after even so extensive a ligation. So far as the utility of such an operation is concerned. it can only be of value in cases where the bacteria seem to be thrown into the circulation in great numbers during the chills, and where ligation is followed by the disappearance of germs from the blood.

VEIT (*Zentralblatt f. Gynäkologie*, 1912, No. 11), believes that pyemia may be diagnosticated with certainty when a puerperal patient has repeated chills. Abdominal section does not militate against the patient. The danger lies in the fact that the tissues about the thrombosed

veins are already infected, and after ligation are not adequately drained. If possible, operation should be done extraperitoneally so far as possible, the endeavor being to lay open the infected focus freely, as well as to ligate the vein. Where the tissues about the veins are found extensively infiltrated, the operation should be abandoned and hiridin given instead. As regards the time of operation, the earlier it is done the more veins must be tied. When operation is performed late, only those veins should be ligated which are evidently thrombosed. Unless one can outline the vessels clearly operation should not be undertaken. In cases where pyemia is complicated by general infection operation will do no good, but on the other hand will do no harm. In discussion, Fromme has observed both the common iliac veins completely plugged without much interruption in the circulation of the lower extremities. He believes that the common iliac can be tied without danger to the patient. He cited Hartmann's paper, in which he described Trendelenburg's ligation of the inferior vena cava in a puerperal patient suffering from pyemia with staphylococci in the blood, the operation proving successful.

BENTHIN from Winter's clinic in Königsburg, (*Zentralblatt f. Gynäkologie*, 1912, No. 39), comments upon Warnekros's paper, and reports two interesting cases of puerperal pyemia from bacteriological examinations. Both cases on admission seemed hopeless, for after endometritis, pyemia declared itself by chills, and in the vaginal secretion and blood streptococci with weak hemolytic power were found. On the thirteenth day of illness the first chill appeared, and on the twenty-third day an extensive thrombosis of the lower extremity. Two days later a second chill occurred, followed by five others at increasing intervals. Bacteria were present in the blood until the twenty-seventh day of the disease, but in progressively lessened numbers. After three months illness both patients recovered. These cases were treated on purely conservative lines without operative interference, even the examinations being limited as much as possible. The patients were given stimulants and abundant food, as the essential elements in treatment.

FINDLEY (*American Journal of Obstetrics*, December, 1912), reports 7 cases of puerperal thrombophlebitis without operation and with conditions which he believes made operation unjustifiable. In the fatal cases autopsy showed that ligation of the veins would not have prevented the spread of septic infection.

Hebostiotomy.—VAN DE VELDE (*Archiv mens. l'Obstétrique*, January, 1912), would limit hebostiotomy to cases of moderate disproportion between mother and child in which but slight increase in pelvic size would be necessary to bring about delivery, both mother and child being in good condition. He alludes to his previous papers upon the subject for the description of his operations. He believes that the operation has a very limited field. The relative importance of forceps, version, pubiotomy and hebostiotomy, in comparison with Cesarean section, may be inferred from the fact that during the past year no extensive and important paper has appeared upon the former operations. Upon Cesarean section alone, in its different varieties, more than thirty papers of differing value have been published. As regards

technique, interest centres in the comparison between the intra- and extraperitoneal methods. The classic section still holds its place as the most widely useful, thorough and comprehensive, of all forms of delivery. When performed upon patients in good condition, its maternal mortality is between 2 and 3 per cent.; its fetal mortality nil. It enables the operator to recognize abnormal conditions in the pelvis and abdomen which demand attention, and places him in a position to deal successfully with them. It is followed by a speedy convalescence, usually uncomplicated, without the interruption of lactation, and leaves the patient in sound condition for further child-bearing. While it is essentially a hospital procedure in emergencies it may be safely done in private houses. It is an operation for experts, and in their hands is remarkably successful. Its application is steadily extending and evidence is accumulating in favor of its selection in accidental separation of the placenta and in central placenta prævia. While vaginal Cesarean section has its advocates, the majority of operators prefer the abdominal route. The advantages claimed for extraperitoneal section are the avoidance of danger following the opening of the peritoneum, the lessened mortality in septic cases, and the prompt recovery without complications, leaving the patient in good condition for subsequent pregnancy. Its disadvantages are the fact that the peritoneum is often opened, that difficulty is sometimes experienced in delivering the child, that hemorrhage is sometimes considerable, and that the uterus is left adherent to the anterior abdominal wall. Extraperitoneal section is frequently practiced in Germany, but less often in other countries.

GYNECOLOGY

UNDER THE CHARGE OF

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Importance of the Lymphatics in Ascending Renal Infection.—Some extremely interesting experimental work in the dertermination of the method by which ascending infection of the kidney from involvement of the lower urinary tract occurs have been recently reported by SWEET and STEWART (*Surg., Gyn., and Obst.*, 1914, xvii, 460). In a general way, the conclusions at which they have arrived concur with those reached, by somewhat different routes, by Bauereisen and Sugimura, both of whose work has been previously discussed in this department. Bauereisen demonstated the existence of a communicating chain of lymphatics, running in and about the ureteral wall, between the bladder and the kidney. Sugimura showed, in a series of autopsy specimens from cases with severe infections of the bladder, that the inflammatory process could be followed up the ureter to the kidney, not, however, by way of the mucosa, which was to all intents and purposes intact, but by way of the *lymphatic channels* in the deeper

portions of the ureteral walls. Sweet and Stewart have attacked the problem by the experimental method. By cutting one ureter, and inserting a length of rubber tubing between the severed ends, they have been able to maintain the patency of the lumen, and at the same time completely sever the lymphatic communication between the bladder and the corresponding kidney. When such an operation was performed, the urethra ligated and cut, and a virulent bouillon culture of colon bacilli injected into the bladder, an infection of the kidney on the non-operated side, with intact ureter, occurred, whereas the kidney into whose ureter the rubber tubing had been inserted remained free. Likewise, when a ureter was severed from the bladder, and passed into the intestinal tract through one of the pancreatic ducts, thus leaving the lumen patulous, but the lymphatics not in contact with virulent infection, no ascending infection occurred, but in all cases in which the ureter was implanted directly into the intestine, prompt renal involvement followed. On the other hand, in several instances, the ureter was isolated for a short portion of its course, but its continuity to the bladder not severed. The isolated portion was then dropped as a loop into the intestinal lumen through an incision in the gut wall, this being immediately closed, with great care, not to constrict the ureter either at its point of entrance or emergence from the bowel. Thus, the ureteral lumen was in no way exposed to intestinal organisms, but the lymphatics were, and in every instance infection of the kidney occurred. Finally, in several experiments, sufficient of one pole of the kidney was cut away to freely expose the pelvis, and this was planted directly into the intestinal wall. In most of these cases no general infection of the kidney substance occurred. From these experiments, Sweet and Stewart conclude that it is by means of the lymphatics, and not by means of the ureteral lumen or the bloodvessels, that ascending infection of the kidney occurs; they do not, however, deny the possibility of hematogenous infection secondary to some focus *outside* the genito-urinary tract.

Unusual Uterine Tumors.—Three cases of very rare, embryonic malignant tumors of the uterus are reported in the *Jour. Obst. and Gyn. Brit. Emp.* for January, 1914. Two of these, described by Glynn and Bell, were "rhabdomyosarcomata," occurring in two women, aged respectively sixty-two and seventy-five years. In each instance the patient had had a bloody vaginal discharge for some time, and had then passed a tumor mass *per vaginam*, following which hysterectomy was performed. In the first case the uterus was enlarged to the size of a three-months' pregnancy, due to the presence of a tumor growing from the posterior wall, which showed microscopically a mixture of small spindle and very large oval or round cells, with somewhat peripherally situated nuclei. These latter were found to be in reality embryonic muscle cells, cut transversely; in places a few of these cut longitudinally were seen, showing here distinct transverse striations. This patient died six months after operation, with symptoms suggesting pulmonary metastases, but no autopsy was performed. In the second case the diagnosis was made from histological examination of the spontaneously discharged polypoid mass, and a panhysterectomy was then done. Three months later the patient returned with symptoms

of intestinal obstruction; at re-operation the abdomen was found filled with recurrent masses, and the patient died ten days later. The polypoid mass in this instance showed a mixed-celled sarcoma, with numerous giant cells and embryonic striped fibers. The growth in the extirpated uterus, on the other hand, was composed entirely of mixed-celled sarcomas. In neither of these cases were areas of cartilage, glands, or other types of tissue present. The third case, reported by Murray and Littler, occurred in a woman, aged forty-six years. She, likewise, had noticed for some time an unpleasant watery discharge; upon examination a soft polyp was seen projecting from the cervix, and was removed, shortly after which a panhysterectomy was performed. The patient made a good recovery, and up to the time of the report (three months later) did not show signs of recurrence. Histological examination of both the polyp and the polypoid endometrium in the extirpated uterus showed an extremely complex aggregation of tissues—the stroma showed all gradations from a fibrosarcoma to spindle-celled and round-celled sarcoma; there were no giant-cells, but scattered throughout the tissue were numerous areas of hyaline cartilage and many gland-like spaces, lined by a single layer of columnar epithelium, and much resembling the normal endometrial glands. No striated muscle fibers were found. The neoplastic process appeared to be entirely confined to the endometrium, no invasion of the musculature being demonstrable. The last-described tumor is called by Glynn and Bell an "adenochondrosarcoma;" it undoubtedly belongs, however, to the same general group as the first two, *i. e.*, to the category of mesodermal mixed tumors, which probably arise from displacements of embryonic mesodermal tissue from the lumbar region during early life. The high grade of malignancy of the majority of such neoplasms is well illustrated by the course of the first two cases.

Abdominal Exercise in the Treatment of Dysmenorrhea.—Mosher (*Jour. Amer. Med. Assoc.*, 1914, lxii, 1297), has been making for a number of years careful clinical and experimental studies of so-called functional dysmenorrhea, and has come to the conclusion that it is in the large majority of cases *congestive* in origin, the chief factors responsible for its production being: (1) the upright position, (2) alteration of the normal type of respiration by disuse of the diaphragm, (3) lack of general muscular development, (4) inactivity during the menstrual period, (5) psychic influences. The long column of blood in the valveless vena cava, associated with lowered general blood-pressure at the time of menstruation, the local blood-pressure in the uterus being raised, however, all tend to produce congestion, which is frequently so excessive as to cause dysmenorrhea. The upright position, lax abdominal muscles, costal instead of diaphragmatic breathing, and constriction of the body by clothing which interferes with the use of the abdominal muscles and diaphragm, all combine to develop and promote this pelvic congestion. To correct this condition, Mosher says she has found the following very simple procedure extremely efficacious: All tight clothing is removed, and the patient is placed on her back, on a level surface, in the horizontal position. The knees are flexed, and the arms are placed at the sides to secure relaxation of the abdominal muscles. One hand is allowed to rest on the abdominal wall

without exerting any pressure, to serve as an indicator of the amount of movement. The woman is then directed to see how high she can raise the hand by lifting the abdominal wall; then to see how far the hand will be lowered by the voluntary contraction of the abdominal muscles, the importance of this contraction being especially emphasized. This exercise is repeated ten times, night and morning, in a well-ventilated room. The patient is warned to avoid jerky movements, and to strive for a smooth, rhythmical raising and lowering of the abdominal wall. Mosher says that in a large number of cases she has seen a disappearance of all pain, and in many instances a reduction in excessive flow will occur after the institution of this simple regimen. She believes that many women would be far better off if they kept up a greater degree of bodily activity throughout the period than is their custom, although of course, this should not be overdone, and in schools and colleges it would certainly be unwise in most instances to permit the girls to continue all their regular gymnastics and athletics at this time. A most important point, in Mosher's opinion, is to bring about an alteration of the morbid attitude of women themselves toward the menstrual function; as she very truly remarks, "If every young girl was taught that menstruation is not normally a 'bad time,' and that pain or incapacity at that period is as discreditable and unnecessary as bad breath due to decaying teeth, we might almost look for a revolution in the physical life of woman."

Relationship of Gynecology to Psychiatry.—As is well known, Bossi and a few followers are strong believers in the theory that many psycopathic conditions, occurring in women, have their origin in faulty functioning of the genital organs, such as alterations in the internal secretory activities of these organs, the condition of retroverted uterus, with metritis, being, in Bossi's opinion, especially important in this respect. As has been previously discussed in these pages, Bossi claims that many cases of suicidal mania and other forms of insanity can be permanently cured by the performance of suitable gynecological manipulations or operations. A most energetic refutation of Bossi's entire idea has been recently put forth by Siemerling (*Monatsschr. f. Geb. u. Gyn.*, 1914, xxxix, 269), who claims that not only are the former's theories with regard to the origin of psycopathic conditions utterly without foundation in fact, but that examination of records of a large series of cases shows that recovery occurred in as large a proportion of women suffering from psychic disorders upon whom no gynecological treatment was carried out as of those who were treated according to Bossi's principles. He emphasizes, moreover, the fact that many psychoses, such as melancholia, amentia, manic-depressive types, etc., tend to spontaneous recovery, and this, following, in some instances gynecological treatment or operation, may easily give the impression of having been the result of such treatment. Siemerling takes the ground that in the routine examination of every psycopathic patient the genital organs should be taken into consideration, as all other organs of the body, and any conditions found which in a mentally normal individual would require treatment, should be treated just as they would be in such an individual without regard to the mental condition; beyond this, however, he does not think that gynecology has any legitimate field in the treatment of cases of mental disease.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF

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Tumor of the Soft Palate Consisting Mainly of Salivary Gland Tissue.—GUTHRIE (*Jour. Laryn., Rhinol., and Otol.*, February, 1914), reports and depicts this case, which consisted of a pear-shaped tumor hanging from the right side of the soft palate of a lad, aged eight years. When cut through the middle after removal the tumor measured 9 mm. longitudinally and 6 mm. transversely, and was found to consist of a mixed salivary gland of the submaxillary type. The reporter had not been able to discover any record of a similar case.

Tonsillectomy in the Upright Position Under Ether.—ROBERTS describes and depicts (*Laryngoscope*, February, 1914) his method of performing tonsillectomy in the upright position under ether, using a Whitehead gag and administering the ether through one of the nasal passages.

Foreign Body (Halfpenny) in an Esophagus of a Child for Eight Years.—PORTER (*Jour. Laryn., Rhinol., and Otol.*, February, 1914), reports the case of a child who had swallowed a halfpenny at the age of four years and retained it in his esophagus for eight years. An *x*-ray photograph showed its presence in the esophagus between the fifth and sixth dorsal vertebræ. An attempt to seize it with forceps under esophagoscopic inspection failed, and the coin slipped out of sight into the stomach. No ulceration or lesion of any kind could be detected in the walls of the esophagus at the point of detention.

Suspension Laryngoscopy in Children.—ALBRECHT (*Jour. Laryn., Rhinol., and Otol.*, February, 1914) states that suspension laryngoscopy in children is much simpler than in adults. The reasons for this he ascribes partly to the upright position of the epiglottis, which often permits of a satisfactory view as soon as the base of the tongue is pressed upon, and partly to the slender build of the neck characteristic of childhood. He states that clinically the procedure has rendered more certain: (1) the removal of the larger infantile nodes ("screamer's nodes"), analogous to the singer's nodes of adult life, and ascribed to habitual crying or screaming; (2) the operative treatment of laryngeal tuberculosis; (3) the operative treatment of papilloma, which he considers its great field, and of which he mentions nine cases thus treated. To these three procedures he adds a fourth, enucleation of the tonsils, stating that in operating under narcosis, and with the head dependent; suspension gives a first-rate view of the tonsillar region, so that enucleation can be effected in a few minutes under the strictest visual control.

Extirpation of the Arytenoid Cartilage in Laryngeal Stenosis.—IWANOFF discusses (*Revue Hebd. de Laryn., d'Otol., et de Rhinologie*, February 21, 1914), dyspnea produced in stenosis of the larynx due to immobilized median position of the vocal cords. He recommends extirpation of the arytenoid cartilage in order to secure and maintain a larger glottis and thus dispense with the permanent use of the tracheal cannula. The operation is described in detail and one case is narrated in which, after considerable tribulation, a satisfactory result ensued.

Resection of the Vocal Cords in Laryngeal Stenosis.—IWANOFF reports (*Revue Hebd. de Laryn., d'Otol., et de Rhinologie*, February 28, 1914) 4 cases of laryngeal stenosis from vocal cords in median position in which he has practised with success, resection of the vocal cords so as to allow the patient to breathe without the use of the cannula. (This is an operation long practised by veterinarians to overcome "roaring" in abductor paralysis of the vocal cords in horses). Iwanoff states that the voice is not much impaired, and sometimes it is even better than is found in many cases of chronic laryngitis.

Histological Examination of the Superior Laryngeal Nerve After Injections of Alcohol.—LANNOIS AND BÉRIEL report (*Revue Hebd. de Laryn., d'Otol., et de Rhinol.*, March 7, 1914) 9 cases in which they examined the superior laryngeal nerve in patients who succumbed a few days after injections of alcohol for the relief of pain in laryngeal tuberculosis. These examinations were controlled by similar examinations in cases of laryngeal tuberculosis who had not been subjected to injections. While the results are not very positive, it may be said that the alcoholic injections but little modified the nerve trunk, because in a number of cases histological differences were rarely to be detected between nerves injected and nerves not injected. It was suggested that this circumstance might indicate that the alcohol was rarely introduced into the nerve itself. On the other hand, it might be inferred that this injection into the nerve does not appear to be indispensable for the therapeutic result. It might be mentioned that when histological modification had been noted it was always periaxial.

HYGIENE AND PUBLIC HEALTH

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Uta.—STRONG, TYZZER, BRUES, SELLARDS, AND GASTIABURU (*Jour. Amer. Med. Assoc.*, November 8, 1913, lxi, 1713) report upon *uta*, a disease which has existed in Peru since prehistoric times, and the

lesions of which have been supposedly depicted on the ancient "huacos" of the Incas. It has been stated by various authorities that the disease represented a form of syphilis, or one of prehistoric leprosy, or a special form of lupus vulgaris. In recent years two extensive monographs on the subject have appeared from Peru, one by Tamayo in 1908 and the other by Palma in 1909. Tamayo regarded the disease as a special form of lupus vulgaris. Palma concluded that it was a specific disease which was not to be confounded with other South American maladies, and that it was not a form of tuberculosis. The present investigation showed that uta is due to a species of Leishmania. The flagellate stage of the organism was obtained, and animals were successsfully inoculated from a human case. In both Surco and Otao (the latter town deriving its name from the prevalence of the disease there) a large proportion of the inhabitants are either afflicted with the disease or show the disfiguring scars which have resulted from a previous attack, on the face, arms, or legs.

Verruga Peruviana and Oroya Fever.—STRONG, TYZZER, BRUES, SELLARDS, and GASTIABURN, (*Journ. Amer. Med. Assoc.*, November 8, 1913, lxi, 1713) report upon two distinct diseases, verruga peruviana and oroya fever, which were formerly considered to be merely different stages of one disease. The disease was supposed to begin with the oroya fever stage, also known as the *fiebre grave* of Carrion, and if the individual did not die in this stage then the eruptive or verruga stage was said to follow. If the eruption was generalized and abundant, it was stated the individual would surely recover. In the chronic or mild type of the disease the severe initial fever was supposed to occur. It appears that the reason for considering the two diseases as merely different stages of one disease was based particularly upon the fact that in 1885 Daniel Carrion, a Peruvian medical student, in trying to solve problems in relation to the etiology of the affection, inoculated himself on both arms with material from a verruga nodule. It is related that twenty-three days later he began to suffer with symptoms of oroya fever, from which complaint he died sixteen days later. However, no accurate record of Carrion's symptoms is available, and no accurate record of the autopsy performed. It has since been suggested that he died of typhoid fever. Numerous organisms have been described in connection with the etiology of verruga peruviana and its so-called oroya fever stage. Barton has described a bacillus as the cause of the fever stage, which was later shown to be a paratyphoid bacillus. Later he reported the presence of bodies in the red-blood corpuscles, which he thought were protozoa. By latter observers these were generally regarded as products of cell degeneration. A number of other investigators have found paratyphoid bacilli in the blood in the fever stage, while others found acid-fast bacilli in the lesions from the skin. A species of Leishmania and one of chlamydozoa have also been regarded as the etiological factor in verruga. Thus at the time the present investigations were undertaken, the etiology of verruga peruviana and its so-called oroya fever stage was not determined. It was first shown that verruga peruviana and oroya fever represent two distinct diseases; that verruga was due to a virus which was transmitted to the rabbit's testicle, and particularly to monkeys, by cutaneous inoculation, while

oroya fever was due to a parasite of the red-blood corpuscles. The parasite in oroya fever produces in man an irregular fever, and in severe infections a rapid and very pernicious form of anemia which results in extreme prostration and frequently in death. The parasites were observed in both fresh and stained-blood preparations. They were either rounded or rod-shaped, the rods measuring from one to two microns in length, and the rounded forms from three-tenths to one micron in diameter. They occurred singly and in pairs, end to end, and also in chains. In preparations stained in Giemsa, rods often showed a deeply red staining granule at the ends, while the rest of the rod frequently assumed a more bluish tint. The organism resembles in some of its characteristics those described for anaplasma or certain species of theileria, as well as for those given for two species of grahamella by Brumpt, but in other respects it differed considerably from these, and was therefore classified in a new genus Bartonella, the name of Bartonella bacilliformis being given to the organism of oroya fever.

Autopsy Findings in the Case of Typhoid Bacillus Carrier.—Messerschmidt (*Zeit. f. Hygiene*, 1913, lxxv, 411) reports the circumstances of an aged, mentally deficient woman, who in August, 1907, suffered from typhoid fever, following which she became a chronic carrier. In the first year subsequent to her typhoid attack, not only the feces but also the urine was infected. The urine then cleared up and the feces continued to show intermittently positive results until the time of her death in 1912. Shortly after the original attack the patient had a purulent pleurisy, from which typhoid bacilli were cultivated. The bacilli persisted, however, in the pleuritic exudate for a few days only. At the autopsy, typhoid bacilli were found not only in the bile but also the wall of the gall-bladder, in the liver, in the neighborhood of the great bloodvessels, in the papillæ of one kidney, and also in one suprarenal capsule. As far as the latter organ is concerned, however, the condition is to be looked at as a secondary typhoid invasion of an old tubercular focus. As was to be expected, furthermore, the bacilli were cultivated also from various portions of the intestinal tract. During life, treatment had been attempted with yoghurt, atoxylsaurem queck-silber, and with typhoid immune serum (Kraus), but without result.

Errata.—The observations of Uhlenhuth and Mulzer (*Arb. a. d. Kais. Gesundh. Amt.*, 1913, xliv, 307), abstracted on page 447 of the March issue of the Journal, were made upon *rabbits*, not upon *dogs*. The same correction applies to the observations of Prausnitz and Stem (*Zentralbl. f. Bakteriol.* 1913 lxix, 545), abstracted on page 448 of the same issue.

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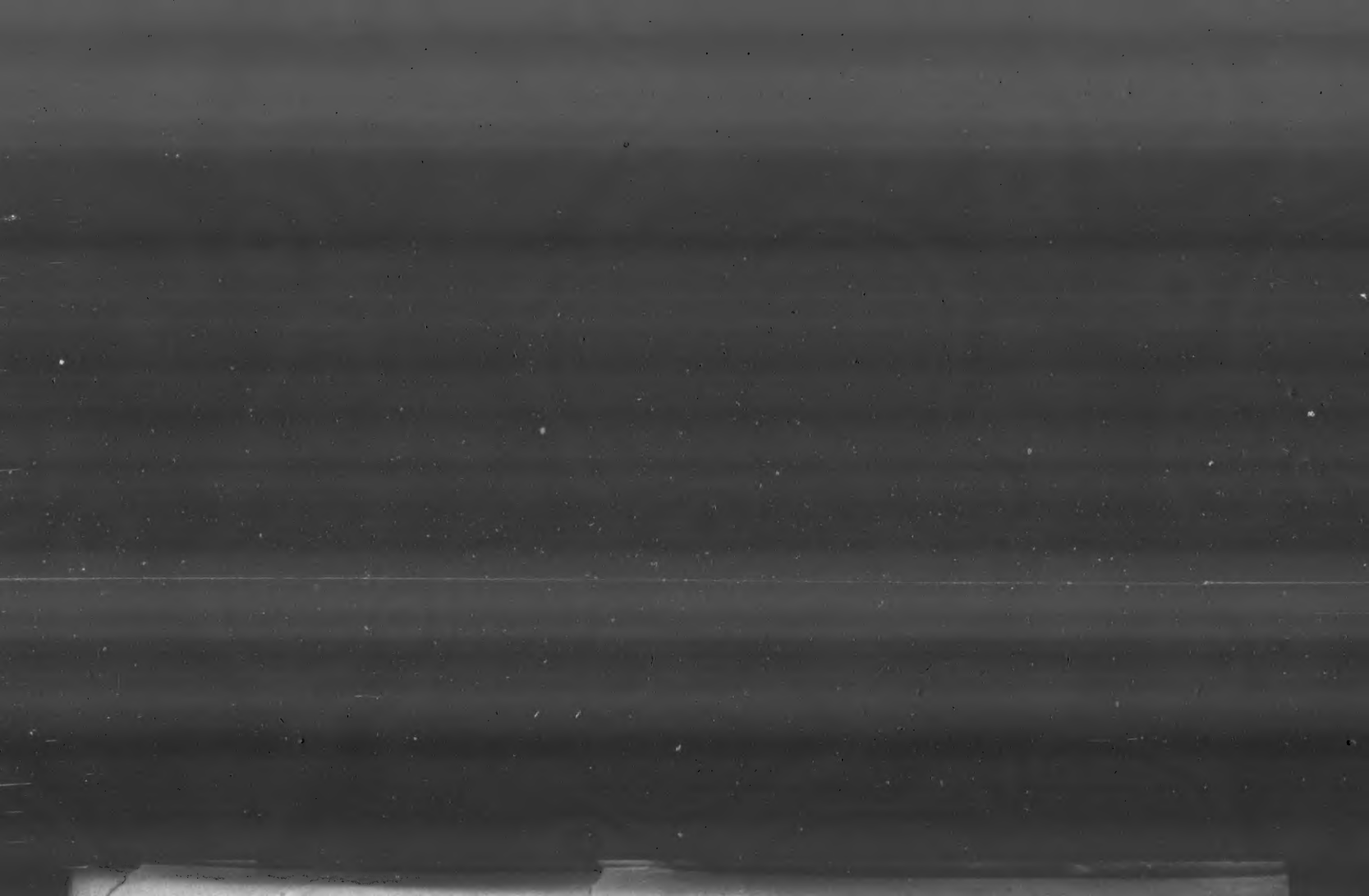
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